PREVALENCE OF DYSLIPIDEMIA IN HIV PATIENTS AND HIV PATIENTS RECEIVING HIGHLY ACTIVE ANTI - RETROVIRAL THERAPY

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CERTIFICATE

This is to certify that this dissertation titled **"THE PREVAL ENCE OF DYSLIPIDEMIA IN HIV PATIENTS AND HIV PATIENTS RECEIVING HAART** " submitted by **DR.ANOOB JOHN K.A.** to the faculty of General Medicine, **The Tamil Nadu Dr.M.G.R. Medical University, Chennai** in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by him under our direct supervision and guidance .

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CONTENTS

INTRODUCTION

HIV infection was first documented in India in 1986 from Chennai[1]. Since then HIV has spread to all parts of the country from the high risk group to the antepartum population in many states[2] at an alarming rate. According to the NACO there are 2.3 million People Living with HIV infection and AIDS(PLHA) in India against the WHO estimation of 5.2 million[2]. UN AIDS estimates show that India belong to low prevalence country according to the latest global report[3]. In 2001 National Behavioral Study conducted among 85000 people, AIDS awareness in India was only 75%[4]. It was particularly low among rural women from Bihar , Gujarat and West B1engal. Less than 33% of all the responders have ever heard of Sexually Transmitted Infections and only 21 % were aware of links between HIV and sexual transmission[4].

With the introduction of Highly Active Anti-retroviral Therapy the longevity of life of the HIV patients have increased up to 50 years if HAART is initiated at an early stage of illness[5] .After the introduction of HAART the chronic complications of the disease and the treatment started appearing more ; including cancers, dyslipidemia, Insulin resistance , lipoatrophy, osteonecrosis, ischemic heart disease [7,8,9,10].

Metabolic derangements and body fat abnormalities are well known to occur in the course of the HIV infection , both due to direct course of the infection and as a complication of treatment[6].

Various studies have addressed on the occurrence of lipodysrophy following HAART (Highly active Anti –Retroviral Treatment) especially with the use of protease inhibitors and NNRTI. characterized by central obesity with peripheral wasting , hyperlipidemia , insulin resistance .[2,3,4,5,]

Abnormalities in lipid metabolism in HIV patient are described before the advent of HAART.[6].Increased serum Triglycerides ,LDL cholesterol and decreased HDL cholesterol is seen in HIV patients in advanced disease especially in HAART treated patients[6] . Abnormalities in body composition is seen in 40- 50 % of ambulatory patients[6] .Recent studies have proved increased incidence cardiovascular mortality mainly following the Protease Inhibitor exposure .[95]. Most of these changes occur in response to HAART especially when viral load is markedly diminished .The risk increases with increasing age, female sex and duration of the drug exposure. Recent studies have shown that there is significant increase in cardiovascular mortality in HIV patients especially on PI & NNRTI based HAART therapy.

The aim of the study is to compare the lipid parameters in patients attending ART centre who are exposed to HAART to patients not exposed to HAART

REVIEW OF LITERATURE

BIOCHEMISTRY OF LIPOPROTENIS[16,17]

Fat absorbed form the diet and lipids synthesized by the liver and adipose tissue must be transported between the various tissue and organs for utilization and storage. Since lipids are insoluble in water, transporting it in an aqueous environment of blood plasma is a problem . This is solved by associating nonpolar lipids with amphipathic lipids and proteins to make water-miscible lipoproteins.

Lipoproteins are composed of lipids, proteins and small amount of carbohydrate. The major lipids in lipoproteins are triacylglycerols, phospholipids, cholesterol, cholesteryl esters and small amount of free fatty acids. The protein moiety of a lipoprotein is called apolipoprotein or apoprotein.

Lipoproteins, consist of a core of cholesterylester, triacylglycerols, and covered by a surface monolayer of phospholipids, free cholesterol, and apolipoproteins. The major plasma lipoproteins-chylomicrons, very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) are

distinguished by lipid content, density on ultracentrifugation, size, mobility on electrophoresis, and the proteins on their surfaces.

The lipoproteins chylomicrons and VLDL are not thought to be atherogenic, but the remnants of their lipolysis chylomicron remnants and IDL, respectively are believed to be atherogenic. The atherogenicity of LDL, the metabolic end product of VLDL and lipoprotein(a) [Lp (a)]has been established, as has the cardioprotective effect of HDL.

All nucleated cells synthesize cholesterol, but only hepatocytes and enterocytes can effectively excrete cholesterol from the body, into either the bile or the gut lumen. In the liver, cholesterol is excreted into the bile, either directly or after conversion to bile acids. Cholesterol in peripheral cells is transported from the plasma membranes of peripheral cells to the liver and intestine by a process termed "reverse cholesterol transport" that is facilitated by HDL

Table :1 Classification of lipoproteins

LIPOPROTEIN CLASS	MAJOR LIPIDS	APO-LIPOPROTEINS	SOURCE
Chylomicron	Triacylglycerol, phospholipids	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E	Intestine
Chlomicron remnants	Cholesterylester, cholesterol	B-48, E	Chylomicron
VLDL	Triacylglycerol, Phospholipid	B-100, C-I, C-II, C-III, E	Liver
IDL	Cholesteryl ester, Triacylglycerol	B-100, E	VLDL
LDL	Cholesterylester, Phospholipid	B-100	VLDL
HDL 2	Phospholipid, Cholesteryl ester	A-I, A-II, C-I, C-II, E	Liver Intestine
HDL3	Phospholipid, Cholesterl ester	A-I, A-II, C-I, C-II, E	Liver Intestine

Apolipoproteins:

The apolipoprotiens (apos) provide structural stability to the lipoproteins and determine the metabolic fate of the particles upon which they reside.

Apolipoprotein	**Mol. Mass (Dalton)**	**Lipoproteins**	**Metabolic Functions**
apo A1	28,000	HDL, Chylomicrons	Structural component of HDL; LCAT activator
apo AII	17,000	HDL, Chylomicrons	Unknown: possibly facilitates transfer of other apos between HDL and chylomicrons
apo B48	2,60,000	Chylomicrons, Chylomicron remnants	Necessary for assembly and secretion of chylomicrons from the small intestine
apo B100	5,50,000	VLDL, IDL, LDL	Necessary for assembly and secreation of VLDL form the liver; structural protein of VLDL, IDL, LDL; ligand for LDL receptor
apo CI	7,600	Chylomicrons, VLDL, HDL	May inhibit hepatic uptake of chylomicron and VLDL receptor

LCAT-Lecithin Cholesterol Acyl Transferase Apoprotein (a), a large glycoprotein that shares a high degree of sequence homology with

the plasma zymogen plasminogen is made by hepatocytes and is secreted into plasma where it forms a covalent linkage with the apo B100 of LDL to form lipoprotein (a). The physiologic role of lipoprotein (a) is not known, but elevated levels are associated with an increased risk for atherosclerosis.

Transport of Exogenous (dietary) Lipoproteins

An average individual consumes 50 to 100 g of fat and 0.5g of cholesterol during three or four meals, hence transport of dietary fats is essentially continual. Normolipidemic individuals dispose most dietary fat in the bloodstream within 8h of the last meal, but some individuals with dyslipidemia, particularly those with elevated fasting levels of VLDL triglyceride, have measurable levels of intestinally derived lipoproteins in the circulation as long as 24h after the last meal.

In the intestinal mucosa dietary triglyceride and cholesterol are incorporated into the core of nascent chylomicrons. The surface coat of the chylomicron is composed of phospholipids, free cholesterol, apo B48, apo AI, apo AII and apo AIV. The chylomicron , essentially a fat droplet containing 80 to 95 percent triglycerides, is secreted into lacteals and transported to the circulation via the thoracic duct. In the plasma apo C proteins are transferred to the chylomicron from HDL. apo CII is required

for hydrolysis of triglycerides by lipoprotein lipase (LPL) on capillary endothelial cells in fat and muscle, and apo CIII may modulate core triglyceride hydrolysis by regulating LPL activity. As a consequence, dietary triglyceride is delivered to adipocytes and muscle cells as fatty acids, and dietary cholesterol is taken up by the liver where it can be used for bile acid formation, incorporated into membranes, resecreted as lipoprotein cholesterol back into the circulation, or excreted as cholesterol into bile. Dietary cholesterol also regulates endogenous hepatic cholesterol synthesis.

Abnormal transport and metabolism of chylomicrons may predispose to atherosclerosis, and their remnants can be taken by cells of the vessel wall, including monocyte-derived macrophages that migrate into the vessel wall from plasma. Cholesteryl ester accumulation by these macrophages transforms them into foam cells, the earliest cellular lesion of the atherosclerotic plaque. If the postprandial levels of chylomicrons or their remnants are elevated or if their removal from plasma is prolonged, cholesterol delivery to the artery wall may be increased.

Transport of Endogenous Lipids

The endogenous lipid transport system conveys lipids from the liver to peripheral tissues and from peripheral tissues back to the liver. In the liver, triglycerides are made from fatty acids that are either taken up from plasma or synthesized de novo within the liver. Cholesterol can also be synthesized by the liver or delivered to the liver via chylomicron remnants. These core lipids are packaged together with apo B100 and phospholipids into VLDL and secreted into plasma where apos CI, CII, CIII and E are added to the VLDL particles.

Triglycerides make up the bulk of the VLDL (55 to 80 percent by weight), and the size of the VLDL is determined by the amount of triglyceride available. Hence, very large triglyceride-rich VLDL is secreted in situations where excess triglycerides are synthesized, such as states of caloric excess, diabetes mellitus, and with alcohol consumption. Small VLDL is secreted when fewer triglycerides are available.

Although VLDL is normally the principal hepatic lipoprotein secreted by most individuals, VLDL and cholesteryl ester-enriched IDL-like particles may be secreted by the liver in individuals with combined hyperlipidemia. Smaller, more dense VLDL particles are efficiently converted to LDL, and apo E in the VLDL remnants is the ligand that the

binds the remnants to the LDL receptor for removal from the plasma. apo B100 is the only protein remaining on the surface of the LDL particle.

The half-life of LDL in plasma is determined principally by the availability (or 'activity') of LDL receptors (apo B100, apo E). Most plasma LDL is taken up by the liver, and the remainder is delivered to peripheral tissues, including the adrenals and gonads which utilize cholesterol as a precursor for steroid hormone synthesis. The adrenals have the highest concentration of LDL receptors per cell in the body. The LDL receptor, a glycoprotein with a molecular mass of approximately 160kDa, is present on the surface of nearly all cells in the body. Goldstein and Brown characterized the molecular genetics and cell biology of the LDL receptor and defined its role in the cholesterol metabolism. While the LDL receptor is a major factor in determining plasma LDL cholesterol levels, the rates of entry of VLDL into plasma and the efficiency with which VLDL is converted to LDL also influence steady-state LDL concentrations in plasma. Increased levels of plasma LDL cholesterol and apo B100 are risk factors for atherosclerosis. Normal LDL does not cause foam cell formation when incubated with cultured macrophages or smooth-muscle cells, but when LDL undergoes lipid peroxidation it becomes a ligand for an alternative, scavenger receptor pathway. Scavenger receptors are present on endothelial cells and

macrophages, uptake of modified (oxidized) lipoproteins by these receptors in macrophages results in formation of cholesterol-laden foam cells. In addition to foam cell formation, oxidized LDL acts in the vessel wall to stimulate the secretion of cytokines and growth factors by endothelial cells, smooth-muscle cells, and monocyte and proliferation of smooth-muscle cells which synthesize and secrete increased amounts of extracellular matrix such as collagen.

The role of VLDL in atherogenesis is uncertain. The major reason for this uncertainty derives from the inverse relationship between elevated levels of triglyceride-rich lipoproteins and reduced levels of the antiatherogenic HDL cholesterol and it is possible that hypertriglyceridemia may not be directly atherogenic but the surrogate of other lipoprotein abnormalities. It is clear that cholesteryl ester-enriched VLDL cause foam cell formation. Thus the risk of atherosclerosis from hypertriglyceridemia and elevated VLDL levels may be determined by the level of cholesteryl ester-enriched VLDL remnants within the plasma. The atherogenic potential of IDL is probably similar to that of VLDL remnants.

LIPOPROTEIN SUBFRACTIONS AND ATHEROSCLEROTIC HEART DISEASE[11]

Hypercholesterolemia

The dyslipidemia clearly associated with increased risk for CAD is hypercholesterolemia, particularly elevated plasma levels of cholesterol carried in LDL. LDL contains approximately 70 percent of cholesterol in the blood and is the primary target of intervention in the guidelines of the third adult treatment panel of the NCEP.

LDL

Small, dense low-density lipoprotein, in addition to LDL cholesterol level, LDL composition influences CAD risk. Small, dense LDL frequently occurs in conjunction with elevated triglyceride level, low HDL cholesterol level, truncal obesity, and hypertension. LDL subclass pattern can be altered to a potentially less atherogenic pattern by pharmacological therapy with gemfibrozil ,for example, has been shown to shift LDL particles toward a larger, more buoyant species. The mechanism by which small, dense LDL causing increased atherosclerotic risk has not been totally determined and may be a combination of mechanisms. Compared with large, buoyant LDL, small, dense LDL has a lower sialic acid content, which may increase the binding capacity of

LDL for proteoglycans localized to the arterial wall. Hemostatic variables may be shifted to a more atherogenic pattern in the presence of small, dense LDL. A dose dependent increase in thromboxane synthesis has been reported with increasing density of LDL particles. Small, dense LDL appears to be more susceptible to in vitro oxidation than large, buoyant LDL. There is overwhelming evidence for reductions in coronary events and cardiovascular mortality with lowering of low-density lipoprotein cholesterol (LDL-C).

Oxidized LDL

LDL may be oxidized as a result of exposure to endothelial cells, smooth muscle cells, or macrophages. Oxidized LDL attracts circulating monocytes, which then adhere to the arterial wall, prevented from leaving the arterial wall scavenger receptors on macrophages recognize and bind oxidized LDL and intracellular cholesterol accumulates. As uptake continues, the macrophages can become lipid-laden foam cells, the components of the fatty streak, which is the precursor atherosclerotic lesion.

Triglycerides (TG)

The Adult Treatment Panel III guidelines suggest that because elevated TGs are an independent CAD risk factor, some TG-rich

lipoproteins, commonly called remant lipoproteins, must be atherogenic. A number of studies have shown that in type 2 diabetes, the severity of CAD is positively related to the numbers of TG-rich particles in the plasma[17]. triglycerides are causally related to the progress of atherogenesis. They are a significant risk factor for CAD in females than males. They continue to be predictors of CAD in both men and women above 65 years[18].

HDL

Plasma levels of high-density lipoprotein-cholesterol (HDL-C) are a powerful independent cardiovascular risk factor, bearing an inverse relationship with atherosclerotic cardiovascular disease. Apart from its protective role in atherosclerosis, HDL-C increased fibrinolysis, is an antioxidant to low density lipoprotein-cholesterol (LDL-C), and decreases platelet aggregation. In particular, HDL carries excess cholesterol from peripheral cells to the liver for removal in the process termed reverse cholesterol transport, reduces oxidative modification of low-density lipoproteins (LDL), and inhibits cytokine-induced expression of cellular adhesion molecules on endothelial cells. Studies of the newly described adenosine triphosphate-binding cassette protein A1 (ABCA1) transporter have established a crucial role for this transporter in modulating the levels of plasma HDL and intracellular cholesterol in the liver as well as in

peripheral cells[20]. Up to a third of patients with atherosclerotic cardiovascular disease have 'desirable' plasma levels of total cholesterol but low HDL-C levels[21].

Metabolic Complications of HIV Infection

Metabolic complications, including dyslipidemia, insulin resistance and altered fat distribution (loss of subcutaneous fat and a relative increase in central fat), are common in adults infected with HIV which is more pronounced in patients receiving HAART[6]. These complications may increase these patient's risk of cardiovascular disease.

Dyslipidemia in HIV

Alterations in serum lipid values have been widely reported among persons infected with HIV. Longitudinal assessment of patients with HIV seroconversion suggests that there are decreases in total, HDL and LDL cholesterol and increase in triglycerides (TG) and VLDL, before treatment[6,12,13]. Sharon. A. Riddler et al., reporting the results of serum lipid levels in 50 HIV positive treatment-naïve patients noted a decline in mean total cholesterol (TC) by 30 mg/dL HDL-C by 12 mg/dL and LDL-C by 22 mg/dL compared to preseroconversion values [13]. Early studies also shown an increase in plasma free fatty acids and a decrease in apolipoproteins A-1 and B-100[23].

Pathogenesis of Dyslipidemia in HIV

Various studies on HIV patients suggested that factors contributing to dyslipidemia were increased apo E levels, increased hepatic synthesis of VLDL and decreased clearance of TG[13,23, 24]. Dyslipidemia may also be due in part to the effect of viral infection, acute phase reactants, circulating cytokines including interferon α (INF α)[25].

Increased rates of VLDL-TG secretion during both fed and fasted condition contribute to hypertriglyceridemia associated with HIV infection[13]. Hepatic fatty acid availability is the major regulator of VLDL-TG secretion[26]. It is likely that the increased basal rate of fatty acid release from subcutaneous adipose tissue stimulates the increase in basal VLDL-TG secretion. HIV infection itself rather than HAART was responsible for the alterations in fatty acid metabolism, because basal glycerol kinetics, an index of adipose lipodystrophy whether receiving HAART or not[21]. It is possible that the greater basal lipolytic rate was the result of increased beta-adrenergic stimulation of adipose tissue[13]. To support this view, it was found that plasma and urinary catecholamines were increased in subjects with HIV[6,28] .

In addition, increased beta-adrenergic stimulation is responsible for increased basal lipolytic rates in other inflammatory diseases, such as

cancer[29]. Increased rates of hepatic denovo lipogenesis have been observed in patients with HIV infection. Therefore it is likely that increased hepatic fatty acid availability and increased denovo lipogenesis contributed to high VLDL-TG secretion[30]. Plasma clearance of VLDL-TG was lower in men with HIV dyslipidemia than is healthy men during both basal conditions and fed state. The reduced rate of clearance may be related to alterations in lipoproteinlipase activity associated with HIV infection or HAART[31,32]. This also contributes to the high VLDL-TG in HIV infection.

Infections are well known to cause metabolic alterations as a part of direct effect of the infection, via release of acute phase reactants and cytokines[33]. Of these, cytokines – especially INF- α was found to have strong association with dyslipidemia in HIV.[14,20] Grunfeld.C. et al reported significant elevation of serum INF- α in patients with HIV positively and AIDS. There was significant correlation between INF- α levels and serum TG level. These studies suggest that INF- α, which has previously been shown to modulate lipid metabolism in vitro and invivo may be responsible for the hypertriglyceridemia found in AIDS.

C-reactive protein levels were increased in AIDS, but tumor necrosis factor and haptoglobulin levels were not[15].

Dyslipidemia in HIV patients on HAART

Dyslipidemia has also been associated with the use of HAART but of a different pattern from that of treatment naïve patients. Protease inhibitors have been mostly implicated but other class of drugs nucleoside reverse transcriptase inhibitors also were found to alter lipid profile. There is an increase in total cholesterol, TG, LDL-C, VLDL, lipoprotein (a), and apolipoprotein B which occur independently of HIV infection [10,34]. Protease inhibitors interfere with cholesterol synthesis, by inhibition of the proteasome, which regulates apolipoprotein B production. It also inhibits sterol regulatory enhancer-binding protein-1 (SREBPI) causing increased hepatic lipid production [35,36]. Dyslipidemia may also be a consequence of insulin resistance, of visceral fat accumulation and of lipoatrophy with release of stored lipids and an inability to take up circulating TG.

Protease inhibitor and efavirenz induce lipoatrophy by inhibiting SREBP1 (Sterol regulatory enhancer binding protein) which mediates activation of Retnoid X receptor, PPARÝ coactivator 1[6]. Except Atezenavir all Protease inhibitors cause lipodystrophy and dyslipidemia. As a result of metabolic complications of PI based regimes they are now used on failure of NRTI based regimes [95 API]

Friis-Møller et al., reporting the results of a large cross-sectional study, noted that hypercholesterolemia(more than 240 mg /dl) in 27 percent of subjects receiving combination therapy that included a protease inhibitor, 23% receiving nonucleosidereverse-transcriptase inhibitor, and 10% receiving only nucleoside reverse-transcriptase inhibitors, as compared with 8 % among the previously untreated subjects. The corresponding percentages for hypertriglyceridemia (more than 200/dl). were 40, 32, and 23 percent, as compared with 15 percent among previously untreated subjects.

Low levels of high-density lipoprotein (HDL) cholesterol(< 35 mg per /dl were reported in 27, 19, and 25 percent of the subjects, respectively, as compared with 26 percent of those who were previously untreated .Among patients with evidence of body-fatabnormalities,57 percent had triglyceride levels above 200 mg/dl, and 46 percent had HDL cholesterol levels below 35 mg /dl , as compared with 9 and 17 percent of healthy subjects matched for age and body-mass index from the Framingham Offspring Study cohort.

For cholesterol levels above 200 mg /dl , the prevalence rate in the HIV-infected group was 57%, as compared with 42 % in the Framingham control group.

Nucleoside analogues causes lipoatrophy and dyslipidemia by mitochondrial injury resulting from inhibition of mitochondrial DNA polymerase of adipocytes. They also inhibit adipogenesis & adipocyte differentiation promote lipolysis and excretes synergistic toxic effect of protease inhibitor[6].Efavirenz based regimes have shown more dyslipdemias and cardiovascular risk compared to nevirapine based regimes. Leonardo Calza; Roberto Manfredi; and et al proved this in their study Nevirapine is a better substitution for efavirenz in PI based regimes.

Storage of increased circulating fatty acids ,impaired fatty acid oxidation contribute to intra myocellular fat accumulation , insulin resistance and hepatic steatosis[6].

Body fat abnormalities and lipodystrophy in HIV

Abnormalities in body composition have been reported in 40 to 50 percent of ambulatory HIV infected patients and the proportion is greater in those receiving HAART[11,36,37]. Prevalence rates vary widely from 11 to 83 percent in cross-sectional studies.[39,40]

Lipoatrophy rates may be even higher depending on the characteristics of the cohort (sex, age, and possibly race), the type and duration of HAART, and the comparison population.[41] Definitions of clinically significant loss of subcutaneous fat and gain in truncal fat have not yet been established. A preliminary case definition based on data obtained by dual energy X-ray absorptimoetry (DEXA) and computed tomography was validated in a prospective study but is not yet recommended for use in clinical practice.[41]

Subcutaneous lipoatrophy and relative or absolute accumulation of central fat may occur in HIV infected patients. Subcutaneous lipotrophy is most noticeable in the face, limbs and buttocks but can also occur in the trunk.[42] Central fat accumulation, when present, most often represents the accumulation of visceral fat. Total abdominal fat accumulation may vary and may occur independently of peripheral fat loss.[41] Fat accumulation may also be found within the breast and over the dorsocervical spine resulting in 'buffalo hump', in lipomata and within the muscle and liver. This pattern of peripheral lipoatrophy and central lipohypertrophy result in increased waist hip ratio (WHR).

Prospective studies investigating body composition in patients starting antiretroviral treatment for the first time have demonstrated initial increase in limb fat during the first few months of therapy, followed by a

progressive decline during the ensuing three years[44,45]. In contrast, truncal fat, increases initially and then remain stable during the ensuing two to three years, resulting in relative central adiposity. Changes in limb and central fat masses are clinically evident in 20 to 35 percent of patients after 12 to 24 months of HAART[46,47].

Pathogenesis of Lipodystrophy

Changes in body composition have been reported in a limited number of patients who have never received HAART, but most changes occur in response to HAART when the viral load is markedly diminished.

It is less likely that the syndrome is a direct effect of HIV. Lipodystrophy is almost exclusive to patients receiving HAART. Also visceral fat accumulation and lipotrophy can improve after protease inhibitor and nucleoside – reverse transcriptase inhibitor switching, without changes in viral load.[10] Also most cohorts have found either a negative association between increasing HIV RNA and lipodystrophy or no association at all.

The type, duration and current use or non use of HAART are strongly associated with severity of lipoatrophy. Combination therapy based on the use of two nucleoside analogue reverse transcriptase

inhibitors and a protease inhibitor is especially strongly associated with severe lipoatrophy.[43]

Protease inhibitors may induce lipotrophy by inhibiting SREBPI-mediated activation of the heterodimer consisting of adipocyte retinoid X receptor and peroxisome proliferators activated receptor γ (PPAR γ) or related transcription factors such as PPAR γ coactivator 1[34.,35]. Invitro studies have demonstrated that protease inhibitors can inhibit lipogenesis and adipocyte differentiation, stimulate lipolysis, and impair SREBPI nuclear localization.[47]

The nucleoside analogue linked most strongly to lipoatrophy is stravudine, particularly when used in combination with didanosine.[14,43] Lipoatrophy associated with nucleoside analogues may be due in part to mitochondrial injury resulting from inhibition of mitochondrial DNA polymerase γ within adipocytes[49] and depletion of mitochondrial DNA[50], although the extent and specificity of this effect remains unknown. Nucleoside analogues can inhibit adipogensis and adipocyte differentiation[51], promote lipolysis and exert synergestic toxic effects with those of protease inhibitors invitro and invivo[52,53].

Older age, lower body weight before therapy, prior diagnosis of AIDS, and a lower nadir CD count are associated with lipoatrophy. Central fat accumulation may be more common among women than among men.[54] Storage of increased circulating fatty acids, impaired fatty acid oxidation, or both may contribute to increased intra-cellular lipid content, hepatic steatosis and insulin resistance.[55,56.57]

Apart from lipodystrophy, generalized wasting can occur in HIV infection. Generalized wasting is an AIDS defining condition. It is defined as involuntary weight loss of more than 10% associated with intermittent or constant fever and chronic diarrhea or fatigue lasting more than 30 days in the absence of a defined cause other than HIV infection. A constant feature of this syndrome is severe muscle wasting with scattered myofibre degeneration and occasional evidence of myositis.[58]

Insulin resistance and abnormal glucose homeostasis

Hyperinsulinemia, a surrogate measure of insulin resistance, is commonly seen in association with excess truncal fat, loss of fat in the limbs, an increased waist-to-hip ratio, and a buffalo hump [96]. Among HIV infected adults with lipoatrophy or fat accumulation, diabetes mellitus was seen in 7.0 percent, as compared with 0.5 percent of otherwise healthy control subjects matched for age and body-mass index by Carr

et al[10]. Impaired glucose tolerance was present in more than 35 percent of HIV infected subjects compared with 5 percent of otherwise healthy control subjects matched for age and body mass index. In a longitudinal cohort study, diabetes mellitus was 3.1 times as likely to develop in HIV infected men receiving combination antiretroviral therapy as it was in control subjects over a three year period of observation. The rate at which impaired glucose tolerance and insulin resistance in HIV infected adults progress to overt diabetes mellitus is not known.[10]

Pathogenesis

Antiretroviral therapy may lead to altered flux of substrates, including free fatty acids, as well as accumulation of intramyocellular lipid, alterations in adipokine levels (e.g., a low level of adiponectin), and reduced PPAR gamma expression in subcutaneous adipocytes; antiretroviral therapy may also contribute to altered glucose homeostasis.[60] Protease inhibitors have been shown to induce insulin resistance in vitro by reducing glucose transport mediated by glucose transporter 4 [61], without affecting postreceptor insulin signalling. The results of clinical studies have suggested that indinavir and lopinavir have short-term adverse effects on insulin sensitivity[62,63]. Delayed but long-term effects, possibly related to changes in body composition, may affect insulin sensitivity[63,62]. Protease inhibitors may also reduced pancreatic

beta-cell insulin secretion,[64] but insulin resistance is the primary defect. Direct effects of nucleoside analogues on glucose metabolism have not been demonstrated, but such drugs may contribute to insulin resistance indirectly through changes in fat distribution.

Clinical Consequences of Metabolic and Body Fat Abnormalities

Metabolic complications, including dyslipidemia, insulin resistance, and altered fat distribution (loss of subcutaneous fat and a relative increase in central fat), are common in adults infected with the human immunodeficiency virus (HIV). These complications may increase these patients risk of cardiovascular disease. The chief risk associated with markedly increased triglyceride levels is pancreatitis.[6] Lipodystrophy can lead to issues of cosmetics and stigmatization.

Cardiovascular Disease

Soon after the introduction of protease inhibitors and non-nucleoside reverse-transcriptase inhibitors for the management of human immunodeficiency virus (HIV) infection, clinicians observed unexpected cardiovascular events among patients receiving these new, combination, “highly active” antiretroviral regimens. Angina, myocardial infarction, and stroke were seen in patients who were relatively young. Providers became suspicious that these events were related either to chronic HIV

infection, since patients were surviving for longer periods than they had in the past, or to the new anti-HIV regimens, which are associated with substantial metabolic abnormalities[35,36].

The Kaiser Permanente Medical Care Program of Northern California compared rates of hospitalization for coronary artery disease and reported that the rate of such hospitalizations among HIV-infected patients, regardless of whether they used antiretroviral agents, was 1.5 times that among their uninfected counterparts.[65] Thus, an emerging body of evidence suggested that as HIV-infected patients were living longer as a result of antiretroviral therapy, cardiovascular disease was developing at unexpected rates.

Friis-Moller and collaborators present data from the prospective, multinational Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study. This study collected data on more than 24,400 patients enrolled in 11 previously established cohorts in Europe, the United States, and Australia. Atherosclerotic events were prospectively identified and independently validated[60]. Over a median follow-up time of 1.6 years through February 2002, 126 patients had a myocardial infarction. Including in their analysis the cumulative duration of drug exposure, the authors determined that during the first four to six years of combination

therapy, there was a 16 percent relative increase in the rate of myocardial infarction per year of exposure to antiretroviral drugs.

DAD study group (Phase II) in same cohort of HIV patients their reported a significant increase in death due to cardiovascular disease . The study showed 346 death due to cardiovascular disease with incidence of 3.45% compared to 1.4% in the matched controls. It must be recognized that as HIV infected patients live longer, their risk of cardiovascular disease, compounded by their preexisting burden of traditional risk factors, inevitably increases. Hypercholesterolemia, older age, smoking, diabetes mellitus, male sex, and a prior history of cardiovascular disease were also associated with an increased risk of myocardial infarction.[65] Some cardiovascular events may have been a consequence of HIV infection, of antiretroviral therapy, or of a synergistic relation among all these risk factors.

Mechanisms of Cardiovascular Disease

Is it plausible that HIV infection itself could promote atherosclerosis through a pro-inflammatory effect on endothelial cells, much like the mechanism that has been hypothesized for other infectious agents such as cytomegalovirus, herpes simplex virus, or Chlamydia. HIV infection promote cardiovascular disease indirectly, by way of the lipid

abnormalities it induces and due to the various drugs. The acquisition of HIV infection is associated with reductions in the HDL cholesterol level as well as reductions in the total cholesterol and low-density lipoprotein cholesterol levels.

Hypertriglyceridemia is associated with disease progression and HIV viremia.[66] Hsue *et al.* reported increased carotid intima-media thicknesses and increased rates of progression over a one-year period in HIV infected adults with a mean age of 45 years as compared with age and sex-matched uninfected controls. Increased thickness of the carotid intima-media was associated with traditional risk factors, including hypertension, hypercholesterolemia and smoking.[66] When assessed by electron beam computed tomography, coronary-artery calcifications have been shown to be more common in patients with HIV infection that in uninfected patients. Increased tissue levels of plasminogen activator and plasminogen activator inhibitor 1 suggest that fibrinolysis is impaired in HIV infected patients.

Is it plausible that the antiretroviral drugs themselves promote atherosclerosis directly or indirectly. Endothelial dysfunction and reduced flow-mediated dilation in association with increased atherogenic lipoproteins have been reported among HIV infected adults receiving

protease inhibitors[69], hypertension is more common in HIV infected patients treated with protease inhibitors, nonnucleoside reverse transcriptase inhibitors, or both then in patients who have never received antiretroviral therapy and is associated with increased body-mass index among HIV-infected patients[70].

Much attention has been paid to the metabolic disturbances attributed to these drugs, which could indirectly promote atherosclerosis. High levels of protease inhibitors may promote the formation of atherosclerotic lesions by increasing CD36 dependent cholesterol ester accumulation in macrophages, a scavenger-receptor pathway that is thought to mediate the formation of atherosclerotic lesions.[71]

In addition, certain antiretroviral agents are associated with insulin resistance. HIV infected patients receiving antiretroviral therapy have also experienced changes in body habitus (lipodystrophy) that have themselves been associated with cardiovascular disease. Thus, treated patients may have lipodystrophy, diabetes, and atherogenic lipid profiles, which could be the routes by which these drugs cause premature atherosclerosis, perhaps in concert with direct toxic effects on the endothelium. Taken in aggregate, the weight of the evidence suggests that HIV infected patients treated with combination antiretroviral regimens

are at increased risk for the development of premature atherosclerotic complications.

To summarize. The mechanisms of vascular in HIV-infected patients are not completely known but may relate to dyslipidemia, insulin resistance, diabetes mellitus, inflammation, impaired fibrinolysis, factors specific to antiretroviral medications, or combinations of these factors.

Pancreatitis

Elevations in TG associated with advanced HIV or associated with HAART have been reported to cause serious pancreatitis, but this has been less well reported in literature.[72,73]

Assessment of Metabolic and Body-Fat Abnormalities

Dyslipidemia

In all HIV infected adults, fasting lipid levels should be measured annually before antiretroviral therapy is initiate, and within one to two months after any change in the antiretroviral regimen.[95] It is important to determine whether there is a family history of dyslipidemia or diabetes and to assess the patient's use of alcohol and of medications known to alter lipid levels (e.g., estrogen). Whenever possible, the antiretroviral medication least likely to worsen lipid levels should be selected for

patients with dyslipidemia. The chief risk associated with markedly increased triglyceride levels is pancreatitis.

Abnormal glucose homeostasis

In HIV infected patients, fasting glucose levels should be determined before antiretroviral therapy is initiated and should be determined annually as well as within a few weeks after any change in the antiretroviral regimen. Weight, the severity of fat distribution abnormalities, and medication history should all be assessed, as should the family history, for the presence of diabetes mellitus. Impaired glucose tolerance and insulin resistance are likely to be present for a variable period before overt diabetes mellitus develops.

Impaired glucose tolerance and hyperinsulinemia are considered cardiovascular risk factors in adults without HIV infection. Thus, an oral glucose-tolerance test or measurement of the fasting insulin level should be considered in HIV infected patients with other cardiovascular risk factors or a family history of type 2 diabetes mellitus.

Body-Fat Abnormalities

Annual assessment of body fat is recommended for adults who begin combination antiretroviral therapy that includes two nucleoside analogues or a protease inhibitor, as well as for any patients who switch

antiretroviral agents. Dual-energy x-ray absorptiometry is useful for assessing fat in the limbs over time. Anthropometric measurements of truncal and limb fat, including measurement of waist, hip, and thigh circumferences, may provide additional information about cardiovascular risk. CT scanning provides information about abdominal subcutaneous and visceral fat. But it is associated with radiation exposure and should not be used clinically for this purpose. No technique has been validated for the assessment of facial lipoatrophy.

Risk Assessment and Treatment Options

Risk-Factor Modification

All potential cardiovascular risk factors, including dyslipidemia, insulin resistance, hypertension, smoking, sedentary lifestyle, weight and family history, should be assessed. It is recommended that dietary and lifestyle alterations, including appropriate interventions for smoking and hypertension, be initiated first; subsequently, therapy with lipid-lowering medications for hyperlipidemia or changes in antiretroviral therapy can be begun, when clinically possible. Insulin-sensitizing agents are recommended for patients with diabetes mellitus and should be considered for those with marked insulin resistance.

Risk factor modification must balance the risk of progression of HIV disease against the potential risk of progression of cardiovascular disease with long-term maintenance of antiretroviral therapy. Although the risk of cardiovascular disease is increasing among HIV infected patients, it is still low and is unlikely to outweigh the substantial benefits of appropriate administration of antiretroviral medications. Cardiovascular risk may be a lesser concern for patients with advanced HIV disease and those with HIV disease that is resistant to antiretroviral drugs. However, in planning risk modification strategies, clinicians may do well to consider effective antiretroviral agents with the lowest propensity to increase glucose or lipid levels.

Lipid-Lowering Drugs

In general, statins (HMG CoA reductase inhibitor) should be used to treat isolated hypercholesterolemia, and a fibrate should be used to treat isolated hypertriglceridemia. Combined statin-fibrate therapy can be considered when the response is incomplete, provided that there is appropriate safety monitoring, including periodic measurement of creatine kinase and aminotransferase levels.[74,75,76]

Until more specific recommendations become available, National Cholesterol Education Program guidelines should be used when lipid-lowering therapy is initiated in HIV-infected patients. Drug interactions,

especially between specific protease inhibitors and statins, should always be considered.[76]

Insulin Sensitizing Drugs

In HIV infected adults with central obesity and hyperinsulinemia, metformin (500mg twice daily) improved insulin sensitivity and decreased visceral adiposity, levels of cardiovascular risk markers (tissue plasminogen activator and plasminogen-activator inhibitor 1) and blood pressure. Rosiglitazone cannot be recommended for general treatment of lipoatrophy at this time, but it may be useful in patients with insulin resistance[76,79]

Growth Hormone

Growth hormone levels are reduced in HIV infected men who have excess visceral adiposity and growth hormone secretagogues (including growth hormone-releasing hormone) may prove useful for increasing growth hormone levels to within the physiologic range and for restoring the distribution of body fat toward normal[81-85]

Surgery and Other Strategies to Restore Body Contours

Injection of various agents has been investigated as therapy for facial lipoatrophy. The most widely used is polylactic acid, a resorbable

molecule that promotes collagen formation and appears to improve the appearance of facial soft tissue, with few complications.[89] Surgery (excision or liposuction) has been performed on some patients who have marked dorsocervical fat accumulation, although fat may reaccumulate within a few months.

Changes in Antiretroviral Therapy

Cessation of therapy with the stavudine or zidovudine generally leads to substantial improvements in limb fat mass. However, if another drug is not substituted, virologic failure is likely. Replacement of a protease inhibitor with nevirapine, efavirenz, or abacavir can effectively reduce total cholesterol,[90-93] LDL cholesterol, and triglyceride levels and increase HDL cholesterol levels. Limited data suggest that insulin resistance may also improve in response to replacement of a protease inhibitor by nevirapine. Protease-inhibitor cessation has not been shown to improve lipoatrophy.[91]

AIMS AND OBJECTIVES

1. To determine the prevalence of dyslipidemia in HIV patients on HAART therapy & compare the various lipid fractions with that of age matched HIV patients not on therapy

2. To assess the anthropometric parameters of HIV patients on HAART to those not on HAART

3. T o compare lipid parameters between the individual drug groups

4. To evaluate the importance of Fasting lipid profile estimation as the part of initial evaluation of HIV positive patients before starting HAART

MATERIAL AND METHODS

Setting : Young adult HIV patients of age from 20-45 years who were attending ART Centre GRH Madurai & HIV patients admitted in medical wards GRH Madurai

Collaborating Department - Anti retroviral therapy centre Madurai Medical College Madurai

Design of study	–	Cross -sectional study
Period of study	-	1 year
Sample size	-	126
Ethical committee approval	–	Obtained
Consent	-	Informed consent obtained
Financial Support	–	nil
Conflict of interest	-	nil

SELECTION & DETAILS OF STUDY SUBJECTS

In this study 126 you patients who were attending the Antiretroviral therapy centre GRH Madurai & Medicine wards were included randomly.

Inclusion criteria

1. Patients selected in random attending ART centre
2. Age group 20 – 45
3. HIV infection confirmed by Triple ELISA testing
4. HAART treatment Groups by Patients on treatment more than 2 years.

Exclusion Criteria

1. Diabetic patients
2. Nephrotic range proteinuria
3. Overt Hypothyroidism
4. Patients on drugs : Antihyperlipidemic Drugs:, Thiazides, Steroids, Beta blockers
5. Patients with liver disease
6. Patients who are diagnosed as hypertensive / CAD before initiating therapy

Age group of 20- 45 years were selected because by 20 years a person attains adult anthropometric proportions and remains more or less static until around 45 years after which age related changes occur especially in the waist circumference and waist hip ratio[94]. The triple ELISA testing according to NACO Guidelines was used for diagnosis for HIV infection .The total number of the patients screened were 142 of which 16 patients were excluded were included in the study.

Patients included in the study were divided into 5 groups

Group -1Patients on D4T +3TC+NVP - (No of patients :13)

Group -2 Patients on D4T+3TC+EFV (No of patients :25)

Group -3 Patients on ZDV+3TC +NVP (No of patients :18)

Group- 4 Patients on D4T + 3TC + EFV (N o of patients :17)

Group -5.Patients not on HAART (No of patients :53)

Data

A Performa was filled up for each patient which included age, relevant history of smoking , alcoholism , hypertension IHD, Cerebro vascular accident, peripheral vascular disease Detailed examination was done including anthropometric measurements. The height was measured barefoot in meters and weight (kilogram) in normal indoor clothing. Waist circumference was measured as the narrowest measurement

between the ribcage and iliac crest .Hip circumference was measured as the largest measurement of the hip over the buttocks. Waist hip ratio was calculated and Blood pressure was recorded with standard mercury sphygmomanometer .The lipid profile estimation was done in ERBA -XL 300 Automatic analyzer.

Estimation of Low density lipoproteins

The LDL cholesterol was estimated by the validated Friedwald formula. The formula hinges on the assumption that VLDL-C is present in concentration equal to $1/5^{th}$ that of the Triglyceride concentration.[13] This assumption is valid for triglyceride levels less than 400mg/dl: thereafter, inconsistencies in the VLDL triglyceride/ cholesterol ratio occur, and the formula cannot be used.

LDL cholesterol = Total cholesterol – (HDL cholesterol + Triglycerides/5) The collected data was analyzed using Epidemiological Information Package (EPI 2002) developed by Centre for Disease Control (CDC) Atlanta in collaboration with WHO Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables.

RESULTS AND OBSERAVTIONS

CHARECTERSTICS OF CASES INCLUDED IN THE STUDY

TABLE -3

CASE DISTRIBUTION

GROUP	No of cases	Percentage of cases
1	13	10.3
2	25	19.8
3	18	14.2
4	17	13.5
5	53	42.2
Total	126	100

126 patients were included in the study and they were divided into 5 groups. Patients on D4T +3TC+NVP included in Group 1 (13), patients on D4T +3TC + EVF Group 2 (25) , patients on ZDV+3TC +NVP in Group 3 (18) , patients on ZDV+3TC+EVF in Group 4 (17) and those patients not on HAART as Group 5 (53)

TABLE 4

AGE DISTRIBUTION OF THE POPULATION

Group	Age Group (in years)								Mean	S.D.
	20-29		30-39		40-49		Total			
	No.	%	No.	%	No.	%	No.	%		
I	3	23.1	8	61.5	2	15.4	13	100	34	5.4
II	4	16	13	52	8	32	25	100	36.6	6.1
III	5	27.8	9	50	4	22.2	18	100	33.8	5.7
IV	2	11.8	9	52.9	6	35.3	17	100	36.9	5.3
Total	14	19.2	37	53.4	20	27.4	73	100	35.4	5.8
'p' value for Groups I to IV	0.2357 Not Significant									
V	20	37.7	22	41.5	11	20.8	53	100	33.8	6.2
'p' value for Group V	0.1155 Not significant									

19 % of the treatment group patients belonged to 20 -29 age group which is less compared to 37.7 % in the non treated group . 30- 39 age group accounted for maximum percentage of treatment groups(53.4%) & non treatment group (41.8%) of patients .40- 49 age group accounted 27.4% in treatment group 20.8% non treated group. The p value is not significant among any of the groups.

TABLE- 5
SEX DISTRIBUTION

Sex	Treatment Groups		Group 5	
	No.	**%**	**No.**	**%**
Male	45	61.6	25	47.2
Female	28	38.4	28	52.8
Total	73	100	53	100
'p'	0.152 Not significant			

In the study males were 61.6% in treatment group and 47.2% in non HAART Group and females accounted for 38.4 %in treatment group 52.8 % in non HAART Group. The p value is not significant

TABLE - 6
MARITAL STATUS

Marital status	Group 1-4 No	Group1-4% No	Group 5 No	Group 5 %
Married	64	87.6%	40	75.5%
Unmarried	9	12.4%	13	24.5%
Total	73	100%	53	100%

In treatment groups 87. 6% and in non HAART treatment group 75.5% are married.

TABLE -7

Parameter	Study Group		Control Group	
	No.	**%**	**No.**	**%**
'p' = 0.3414 Not significant				
Smoking				
Non smoker	31	42.5	27	50.9
Smoker	14	19.2	14	26.4
Quit smoking	8	38.4	12	22.6
'p' = 0.5583 Not significant				
Alcoholism				
Non alcoholic	64	87.7	35	66
Alcoholic	9	12.3	18	34
0.0069 Significant				

Non smokers, smokers and people who quit smoking in the HAART groups are 42.5%,19% , 38.4% respectively . In non HAART treatment group 5 the percentage of non smoker , smokers and people who quit smoking are 50.9% , 26.4% and 22.6% respectively.

Alcoholism in HAART group is 12.3% % against 34% in non HAART group. p value is 0.0069 and significant.

TABLE - 8

OTHER PARAMETERS

Parameter	Study Group		Control Group	
	No.	%	No.	%
Hypertension				
Hypertensive	9	12.3	6	11.3
Normotensive	64	87.7	47	88.7
'p' = 0.9185 Not significant				
IFG/ IGT				
IFG present	2	2.7	2	3.8
IGT present	7	9.6	1	1.9
Normal	64	87.7	50	94.3
'p' = 0.5583 Not significant				
IHD				
IHD Present	12	16.4	2	3.8
No heart disease	61	83.6	51	96.2
'p' = 0.051 Not significant				

Hypertension was present in 12.3% in study group compared to 11.3% HAART Group .P value not significant IFG was present in 2.7% study group while in non HAART group is 3.8 % p value not significant IGT was present in 9.6% and 1.9% HAART group and Non HAART group respectively. P value non significant.

TABLE – 9

Parameter	Study Group		Control Group	
	No.	%	No.	%
IHD				
IHD Present	12	16.4	2	3.8
No heart disease	61	83.6	51	96.2
'p' = 0.051 Not significant				

IHD were present in 16% of HAART group and 3.8% in non HAART group. The p value is not significant.

TABLE - 10
BMI

BMI	HAART Group (I,II,III &IV)		Non HAART Group (V)	
	No.	%	No.	%
Underweight	27	37	14	26.4
Healthy weight	44	60.3	39	73.6
Overweight	2	2.7	-	-
Total	73	100	53	100
Mean	19.47		19.56	
S.D.	1.96		1.8	

Mean value for BMI in HAART groups is 19.47 and 19.56 for Non HAART group The p value is not significant(0.50).

TABLE -11

MEAN CD- 4 COUNT OF HAART AND NON HAART GROUP

CD 4 COUNT	HAART GROUP	NON HAART GROUP
Mean	164.1	224.6
SD	53	91
p	0.001 significant	

Mean CD-4 cell count among the HAART groups is 164.1 and in Non HAART group is 224.6. The p value is significant.

TABLE-12

CD- 4 CELL COUNT AMONG THE STUDY GROUPS

CD4 CELL COUNT	HAART Group I,II,III,IV		Non HAART Group V	
	No.	%	No.	%
< 50 (A)	6	8.2	5	9.4
50-200 (B)	43	58.9	14	26.4
200-350 (C)	22	30.1	29	54.7
>350 (D)	2	2.8	5	9.4
Total	73	100	53	100

58.9% of the HAART group and 26.4% non HAART group belong to 50-200 cell group while 30.1% in HAART and 54..7% in non HAART had CD -4 cell count in 200-350 range.

TABLE-13

WAIST / HIP RATIO

Waist / Hip ratio	Treatment Group (I,II,III &IV)		Untreated Group (V)	
	No.	%	No.	%
Normal	12	16.4	19	35.8
Abnormal	61	83.6	34	64.2
Total	73	100	53	100
Mean S.D.	0.952 0.068		0.875 0.06	
'p'	**0.0001 Significant**			

Mean value for Waist / Hip ratio in HAART groups is .0952 and for non HAART groups is .0875 .The p value is very significant.

TABLE - 14
BMI AND WAIST / HIP ABNORMALITIES

Parameter	Normal		Abnormal	
	No.	%	No.	%
BMI	71	97.2	2	2.8
Waist/Hip ratio	12	16.4	61	83.6
'p'	**0.0001 Significant**			

Percentage of abnormal BMI in HAART groups was 2.8% and that of abnormal Waist/ hip ratio 83.6% .The p value is significant.

TABLE - 15

LIPID PROFILE IN STUDY GROUPS. I-IV

Lipid	I		II		III		IV		V		'p' value for Groups I to IV and Group V
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
TC	196.3	26.2	244.5	32.9	178.2	15.7	220.2	23.6	168.5	30.8	0.0001 Significant
TGL	187.5	53.7	231.9	81.1	175.7	63.1	230.4	66	178	68	0.0403 Significant
LDL	121.6	23.1	168	23	102	11.1	138.4	21	93.9	26.4	0.0001 Significant
HDL	37	3.4	36.4	4.7	38.9	4.5	36.2	3	37.3	4.9	0.4189 Not Significant
VLDL	37.5	11	45.5	17.1	35.1	12.6	45.9	13.3	35.6	13.6	0.0163 Significant

Mean values for Total Cholesterol in Group I is 196 mg% ,Group II is 244.5 mg%, Group III is 178.2 mg % , group IV is 220.2 % and Group V is 168.5 %. P value for group I-IV HAART groups to Group V is significant.

The mean values for LDL for Group I is121 mg% , Group II is 168 mg% , Group III is 102 mg% Group IV is 138.4 mg % and Group V 93.9 mg% .The p value of HAART Groups to Group V not on HAART is significant.

Serum Triglycerides mean values for Group I , Group II ,Group III, Group IV and Group V are 187.5 mg% , 231.9mg % , 175.7mg%, 230.7mg% 178 mg% respectively .The p value of Group 1-IV to Group V is (0.040) is significant.

Serum HDL mean values for group I group II ,group III ,group IV and group V are 37 mg% , 36.4mg%, 38.9mg % ,36.2 mg% and 37.3 mg% respectively. p value is not significant. The mean values for mean VLDL values in Groups I to V are 37.5mg%, 45.5mg% ,35.1 mg% ,45.9 mg% and 35.6 mg% . The p value is significant (0 .016)

DISCUSSION & COMPARATIVE ANALYSIS

The global pandemic HIV infection & AIDS is virtually reported from all countries with a global prevalence of 33.2 million and incidence of 2.5 million new cases every year[2]. After the introduction of HAART (Highly Active Anti Retroviral Therapy) & effective control of opportunistic infections patients with HIV infection and AIDS are surviving a longer period of life [5]. As a result of this chronic complications of HIV infection and HAART is being recognized more .Metabolic body fat abnormalities are increasing in HIV population especially in patients on HAART [6,10,35].These include dyslipidemia, lipoatrophy, IFG ,IGT and abdominal obesity which are known risk factors for cardiovascular disease[10] . This study aims in comparing the dyslipidemia in HIV patients on HAART to HIV patients not on HAART.

HIV prevalence in India according to HIV Sentinel Surveillance in 2007 by NACO estimated a prevalence of 2.31 million of PLAH (People Living With HIV and AIDS)in India.[3] Females constitute around 39% of the burden (0.9 million).[3] Children below 15 years constitute 3.5% of the estimated number of PLHA while elderly people with age greater than 49 years constitute 7.8%. Adults aged 15-49 years constitute 88.7% of the estimated number of PLHA

The study was conducted in adult patients attending ART centre and Department of Internal Medicine Madurai Medical College. In this

study the age group selected was from 20-49 which is the most common age group affected by the disease and for the purpose that lipid abnormalities are more common in these age group.[3,94]

Age distribution showed maximum prevalence in the 30 -39 age group among HAART groups I-IV(52%) and non HAART group V (48%).There was no statistically significant difference in age distribution among the groups. [2,3]

There was no significant difference in the sex distribution among the population. Sex distribution in this study showed 61.6% males 38.4 % females in study group 1-IV and in group V is 47.2% and 52 .8% . There was no statistically significant difference in sex distribution but study Groups showed values similar to those in HIV Sentinel surveillance 2007 done by NACO[3] and UNAIDS report 2008[2].

In this study active smokers were 19.2 % in HAART groups and 26.4 %. in GROUP V. Those who quit smoking was high among the HAART group (38%) compared to the non HAART group (12%) . Most of the non smokers are women 87.5% in HAART groups and 92.5 % in non HAART group. In the HAART groups 62.2% of the males where smoker who quit smoking compared to 42 % in the non HAART group. There was no statistically significant difference in the smoking pattern. National sample survey showed 61.3% of tobacco users in rural & 40.7 % in urban areas in India[97]

In this study 97 % of the males are smokers with 62.2 % quit smoking. This high prevalence may be attributed to the high risk behavior of these patients.

Prevalence of alcoholism in HAART group is 12.3 against 34% in non HAART. Alcoholics with abnormal liver functions were excluded from study This difference in the prevalence is due to counseling for ART therapy which helped the patients to quit alcohol. p value comparing the HAART group and the non HAART group is significant 0.069. According to the study of Nuefeld KJ etaland National sample survey 1993-95 showed a prevalence of Alcohol use in 4.5 % of the population which is lesser than those on HAART treatment 12.3% and 34 % in non HAART group. All the females were non alcoholics .[4]

The patients of both groups were divided on basis of CD-4 counts as A ,B,C,D groups with counts <50,50-200,200-350 and >350 cell/mm^3 respectively. The prevalence of very low CD -4 count is 8.2% and 9.4% in the HAART group and non HAART group respectively.58.9% of HAART group and 26.4% non HAART patients were in group B while 30% of HAART group and 54% non non HAART group belonged to category C.Mean p value for non HAART group(224/mm^3) was higher than HAART group (164 /mm^3) .The p value was significant between the HAART and non HAART groups. There was no significant difference in

in CD-4 cell count distribution among the treatment groups and no significant relation was found with lipid alterations in this study.

In this study prevalence of hypertension was 12.3 % in HAART groups and 11.2 % in non HAART group. Study from urban Chennai, Mohan et al[62] reported 8.4% prevalence of hypertension among men and women aged 20 years and above and belonging to the low socio economic group (based on household income, occupation and dietary pattern). Similarly, in the middle socio economic group had a higher prevalence (15%) conducted in 1996-97 .There is increased prevalence noticed in the group IV (17.5%) group I (15%) but not statistically significant.

In 2000, Ramchandran A Snehalatha C *et al* Diabetes Epidemiology Study Group of India(DESI study) a multi centric study[101] involving six urban cities in India (Chennai, Bangalore, Hyderabad, Mumbai, Culcutta and New Delhi) among the age groups of 20 and above showed a prevalence of 14% among men and women (sample size: 5288 men; 5928 women).

In this study six patients were excluded from study according to exclusion criteria. 2 patients(2.7%) in HAART groups was detected to have IFG and 7 (9.6%) patients had IGT compared to 2 cases of IFG(3.8%) and 1 case of IGT(1.9%) in non HAART group. This was not statistically significant . Carr *et al*. reported a 7% incidence of new-

onset diabetes among HIV patients as diagnosed by a two-hour blood glucose value>200mg/dl after administration of an oral glucose tolerance test .[10] IGT and IFG which are forerunners of diabetes, were found in 12.3% in the study group after excluding diabetes cases from the study as against 12 % in urban Chennai population [10] and 13.2% in South Asian population according to International Diabetes Federation.

Abnormalities in body composition have been reported in 40 to 50 percent of ambulatory HIV-infected patients, according to Lichtenstein KA, Ward DJ *et al*.[11,12] The proportion is greater in those receiving combination antiretroviral therapy.[11] The physical appearance of lipodystrophy is more apparent usually by 2 years of HAART therapy [6,12]. With the increase of life expectancy ,HIV patients treated with HAART reaching up to 49.5 years when treatment is started at the age of 20 years[11]. Prevalence rates of lipodystrophy vary widely, from 11 to 83 percent, in cross-sectional studies.[10,] Anthropometric parameters are important tools for measurement of lipodystrophy including weight ,BMI, Waist / Hip ratio, skin fold thickness[6].

Many of the studies failed to show good correlation with lipoatrophy and anthropometry [6] . Jean-Guy Baril, Patrice Junod, Roger LeBlanc *et al* in their study found a weak correlation with lipodystrophy and Waist / Hip ratio in HIV patients on indinavir and stavudine.[28]

In this study 30.4% of the HAART group and 26.4% of the non HAART group were underweight and 62 % in HAART and 68% in non HAART had a normal BMI..2.7% in HAART group and 5.6% in non HAART group are overweight but have no statistical significance. Lichtenstein KA, Ward DJ et al in their study concluded that a decreasing BMI rather than increasing BMI ,increased Triglycerides , older age and female sex are more prone for lipodystrophy.[10]

Mean BMI values for the study in all the groups were between 19.5-19.9. P value was not significant among the HAART groups and also relating to the non HAART treatment groups.

Waist Hip ratio value analysis showed a mean value in the HAART group between 0.932-0.96 which is above the guideline values for men(> 0.90) as well as women(>0.80). The mean Waist / Hip ratio for the non HAART group was found to be 0.875 in which 64% had an abnormal values. There was no statistically significant difference among the treatment groups but significant in comparison to non HAART group. The p value for the treatment groups to non HAART group was significant.(p- 0.001).

This shows Waist /Hip has significant relation to long standing illness and abdominal obesity. There was an increase in Waist / Hip ratio by 0.07 between the HAART groups and non HAART groups which is statistically significant.[102]

Considering the anthropometric measurements observation in this study is that Waist /Hip ratio is a better parameter for assessing the visceral adiposity. Low BMI reflects the weight loss in with progression of disease and an increasing Waist Hip ratio denoting the visceral adiposity. The p (0.001) value is statistically significant.

The DAD Study Group (Data Collection on Adverse Events of Anti-HIV Drugs) by Jens Lundgren and et al in Copenhagen have done extensive studies in the growing metabolic complications in HIV from 1999**.** They have demonstrated a definite association between combination antiretroviral therapy and the dyslipidemia and cardiovascular risk. Its is an International collaboration study including investigators from all parts of the world in an HIV patient cohort of 24,437. During the first phase of study they demonstrated increased dyslipidemias and cardiovascular risk is increased in HIV patients especially with PI and NNRTI based HAART on a 4 year follow up.

The second phase they proved an increased incidence of (345 deaths) cardiac events including myocardial infarction in the 94,469 patients years Incidence of cardiac events was 3.65 /1000 population . The incidence of myocardial infarction increased from 1.53 per 1000 person-years in those not exposed to protease inhibitors to 6.01 per 1000 person-years in those exposed to protease inhibitors for more than 6 years. After adjustment for exposure to the other drug class and established

cardiovascular risk factors (excluding lipid levels), the relative rate of myocardial infarction per year of protease-inhibitor exposure was 1.16, whereas the relative rate per year of exposure to non nucleoside reverse-transcriptase inhibitors was 1.05 . [10,95,96]

E Frontas , Friis Moller *et al* in their study (DAD study first phase) found that dyslipidemia occurred in patients among all HAART groups including Protease inhibitor , NNRTI as well as NRTI. Patients on Protease inhibitor especially dual protease inhibitor had more lipid abnormalities.

The mean values for patients on Single PI therapy ,total cholesterol was 204 mg%, LDL 139.2 mg %, HDL 38 mg% and TG 159 mg% .In patients treated with double PI regime the mean values were 220mg%, 148mg%, 38 mg% and 221 mg% respectively.

In NNRTI based regimens the means values were TC 197 mg%, LDL 123 mg% ,HDL 40 mg% and TGL 115 mg% .

In our study none of the patients received PI based regimes but all the 73 patients in study Group I-IV were on 2NRTI + 1 NNRTI based regimes. The mean value of total cholesterol is 213 .9 mg% in HAART treatment group(1-4) compared to 168.5 in the non HAART group (5) . The p value is significant 0.001 .

The mean LDL values are 136.6 mg % and 93.9 mg% among respective groups. The mean TGL and HDL values are 209 mg % ,178

mg % and 37.1 mg% and 37.3 mg% among the HAART and non HAART groups respectively. Except for HDL all the lipid parameters showed statistical significance when the HAART groups were compared to non HAART group .In the DAD study group values of mean total cholesterol and LDL were less compared to this study but showed similar elevation. This may be attributed to the difference in the study population as DAD study was conducted in European and North American population while this study is in Asian population who are inherently prone for Metabolic syndrome & dyslipidemias.[70,95,96]

In DAD study the percentage of total cholesterol elevated above 240 mg% i.e. (high level) was 23 % among HAART group and 8 % untreated patients . In this study values of TC above 240 mg% are 24.7% and 5.7% .The TGL was elevation in DAD study group is 32 % and 15% in HAART & untreated group respectively.[10] In this study the TGL elevations are 45 % and 30 % respectively. This increased value may be due to combined effect of NNRTI + NRTI as well as the difference in the population as South Asians populations are more prone for Metabolic syndrome and hypertriglyceridemia. HDL less than 35 mg% was seen in 25% of both groups in DAD study while it was seen in 29 % in this study in HAART treatment group and 21 % in non treatment group.

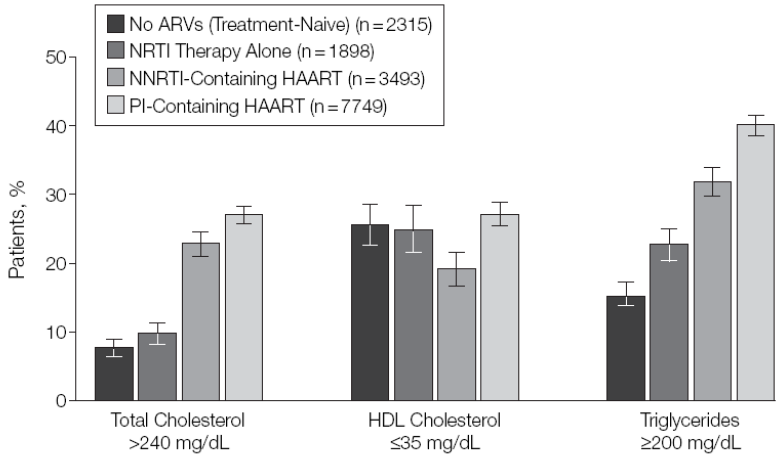
Margaret May, Jonathan A C Sterne, Martin Shipley, Eric Brunne *et al* in their study of 13300 HIV infected men who are aged 40-70

were divided into two groups parametric model based on the Gompertz distribution generalized best. Variables included in the model were systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglyceride, glucose, diabetes mellitus, body mass index and smoking status. Compared with patients not on HAART, the estimated CHD hazard ratio (HR) for patients on HAART was 1.46 for moderate and 2.48 for severe metabolic complications. The study also showed that the hazard ratio for those with severe lipid abnormalities was more (2.46) than in smokers (2 .0).

Analysis of the data in this study showed that all the lipid parameters abnormalities where more pronounced in the group which had nevirapine and stavudine compared to efavirenz and zidovudine based regimes. The Group II followed by Group IV Group I and Group III had decreasing order of lipid abnormalities which was noticed in the study.

The mean total cholesterol was 244.5 mg% , 222mg%.196 mg% 178 mg% in the Group I, Group IV Group I and Group III respectively. The p value is significant .Similarly there was statistically significant increase in LDL , TGL and VLDL. There was also a decrease in HDL which was not statistically significant.

Figure 3. Percentage of Patients With Abnormal Serum Lipid Levels as a Function of Antiretroviral Therapy Regimens



The percentage of patients with elevated total cholesterol, triglycerides and decreased high-density lipoprotein (HDL) cholesterol is shown by the class of antiretroviral drugs (ARVs) . Data are from (DAD) Study Group in 2003.

Randomized control study for a period of three years in 600 HIV patients with two different regimes was done by Joel E. Gallant, Schlomo Staszewski *et al* . The results of the study showed that Tenofovir+ Efavirenz+ Lamuvidine regime compared to Stavudine + Lamuvidine+ Efavirenz regime was equally effective in reducing viral load with significantly less lipid alterations.

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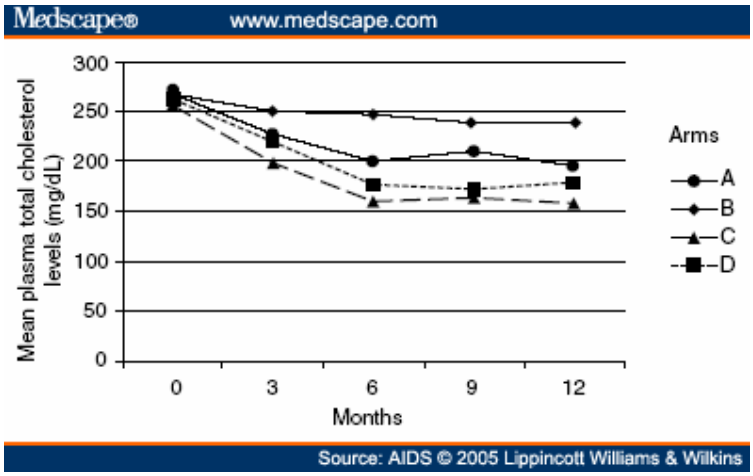
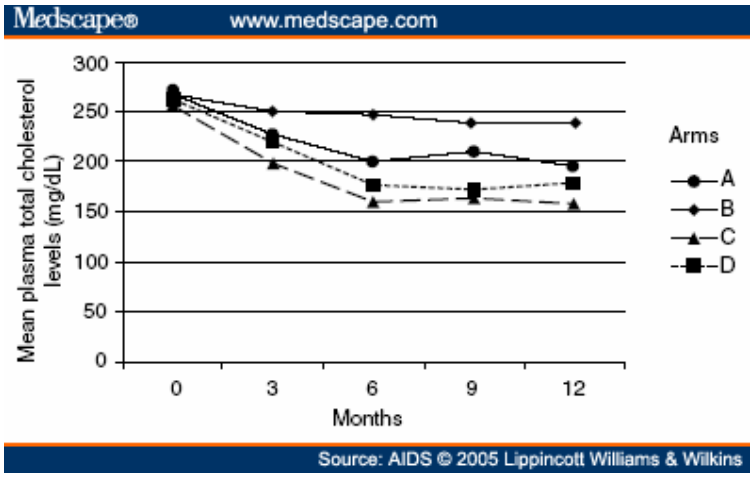
Stephen J Kerr ,Chris Duncombe *et al* in their study reported dyslipidemia in Asian HIV patients after treatment for two years in Thailand. The study was done in treatment naïve HIV population who were started on Protease Inhibitor-containing regimen , stavudine based NNRTI regimen and zidovudine based regimes . Results of the study showed that PI based regimen had more lipid abnormalities than non Stauvidne based NRTI + NNRTI regimes[94].

Leonardo Calza; Roberto Manfredi; *et al* studied the difference of lipid abnormalities in HIV patients on PI based regimens with two different NNRTI- efavirenz and nevirapine .The study was done in treatment naïve 696 HIV patients . 107 patients where selected form the total population who had mixed dyslipidemias following PI therapy after 6 months . They were randomized and was followed up for 6 months.[95,96] The study included 4 arms A- nevirapine arm B efavirenz arm C- pravastatin arm and D- Bebzofibrate arm .





The result of the study showed patients on nevirapine arm did well in both Triglyceride arm Total cholesterol causing a lowering of both parameters by 23% and 29 %. while in efavirenz based arm the results was 9 % and 11% reduction after switching from PI based regimes.[94,95]

Similar observation in our study is that lipid profiles in Group I (nevirapine containing) compared to Group II ((efavirenz based) regimen. In this study the total cholesterol levels in GroupII is 244 mg% and 196 mg% in Group I; similarly Triglycerides are 231 mg% and 181 mg% in the respective groups.The p value is statistically very significant. Similar results was obtained in lipid levels comparing Group III (nevirapine based) to Group IV (efavirenz based) . Total cholesterol is 220 mg% in Group IV and 178 mg% in Group III while triglycerides values are 230 mg% and 175 mg% respectively.

This results clearly shows a more abnormal lipid profiles in efavirenz based regmies than nevirapine containing regimes. Nevirapine

is a better drug substitution for PI in patients with multiple risk factor for cardiovascular event[94,95]. The study also shows that non stavudine based regimes have more lipid abnormalities than zidovudine based regimes [103]. In this study the Group I (stavudine based) has more lipid abnormalities compared to Group III (zidovudine based).

Atherogenic Index of the plasma is the ratio of total triglycerides and HDL and a value below 5 is desirable. In our study the Atherogenic Index was 6.37 for Group II &IV , 5.05 for Group I , 4.5 for Group III and 4.7 for Group V. Mean value among the HAART group is 5.57 and is statistically significant to non HAART population with p value 0.002.[95 ,96]

Total Cholesterol to HDL ratio in this study is 5.29 in Group I, 6.7 in Group II ,4.54 in Group III, 6.07 in Group IV and 4.5 in Group V. In the DAD study the mean values TC:HDL ratio was 3.9 in treatment naïve group and 5.3 in HAART treatment Group.[96] This shows the increased Atherosclerotic and cardiovascular risk in these population.

CONCLUSION

1. Significant Metabolic and morphological alterations occur in HIV infected patients especially in patients on Highly Active Anti-retroviral Therapy.

2. There is a statistically significant increase in the total cholesterol, Triglycerides LDL cholesterol .There is statistically insignificant decrease in HDL cholesterol in HIV patients on HAART .

3. There is an increased prevalence of hypertension and IGT in the HIV patients on HAART .There is an increase in the prevalence of IHD in the treatment groups compared to non HAART group.

4. Increasing BMI is a poor indicator of visceral adiposity and dyslipidemia in HIV patients on the contrary it decrease with increasing dyslipidemia. Waist Hip ratio shows significant correlation with visceral adiposity and dyslipidemia.

5. Dyslipidemia is more in the efavirenz based as well as stavudine containing regimes compared to nevirapine and zidovudine containing regimes .

6. The study doesn't include PI based regimes which has more impact on metabolic parameters.

7. Base line Anthropometric and metabolic assessment including lipid profile, fasting blood sugar should be done as initial workup in every newly detected seroconverters as well as in patients planned for HAART therapy.

SUMMARY

This prevalence study was conducted in the background that dyslipidemia and cardiovascular mortality is reported to increase in HIV patients especially on Anti-retroviral therapy. In this study 126 patients who were attending the Antiretroviral therapy centre GRH Madurai & Medicine wards were included and divided into five different groups according to the anti retroviral therapy after obtaining Ethical Committee clearance from the institution .Patients with HIV infection were initiated on Anti-retroviral therapy based on WHO guidelines. Patients who were exposed to HAART for more than 2 years were selected in the treatment group and compared to age and sex matched treatment naïve group. Biochemical and anthropometric analysis were done and results entered in master chart which was statistically analyzed using computer and EPI 2002 software.

The results of the study showed an increased prevalence of disease among the 30-39 age group with increased prevalence a among males in the HAART groups. The Anthropometric parameters on analysis showed a mean BMI of both HAART and treatment naive Groups in the low normal range. Waist Hip ratio revealed mean of 0.952 HAART groups and 0.875 in treatment naïve group. This showed a significant correlation to Waist hip ratio and the disease while fall in BMI was seen rather than an increase in BMI .

The lipid analysis showed a significant increase in the total cholesterol, LDL and VLDL in both the HAART groups and treatment naïve groups. There was an insignificant fall in HDL levels in both groups. The abnormalities in lipid were more in HAART group especially the stavudine and efavirenz based regimes. When both drugs were present together as in Group II, patients had the maximum alteration in lipid levels.

The Group II followed by Group IV Group I and Group III are in decreasing order of lipid abnormalities noticed in the study. The mean total cholesterol was 244.5 mg% , 222mg%.196 mg% 178 mg% in the Group II, Group IV ,Group I and Group III respectively p value is significant .Similarly there was statistically significant increase in LDL , TGL and VLDL.

On basis of many studies now PI are now reserved for failure of primary regimen .Patients on PI developing metabolic derangements nevirapine is a better substitute than efavirenz. Similarly studies have show proven benefit by switching stavudine with tenofovir and abacavir with equally good viral suppression and less dyslipidemia.[101]

The strategies like screening and monitoring the lipid every 6 months , switching to lipid friendly drugs , lipid modifying drugs as well as change in life style may help to nullify the increased cardiovascular risk and mortality in HIV patients.[96]

BIBLIOGRAPHY

1. Simoes EA, Babu PG, John TJ, Nirmala S,Solomon S, Lakshminarayana CS. Evidence of HTLV-III infection in prostitutes in TamilNadu (India). Indian J Med Res 1987;85:335-8.
2. UNAIDS Report on Golbal AIDS Epidemic International AIDS Conference Mexico City 2008.
3. HIV Sentinel Surveillance and HIV Estimation in India 2007 A Technical Breif National AIDS Control Organisation
4. National Behavioral study 2001HIV and AIDS; AIDS awareness among Indain Adult Population National AIDS Research Institute (NARI) Pune
5. Robert Hogg, Jonathan AC et al The Antiretroviral Therapy Cohort Collaboration study Lancet 2008; 372: 293–99
6. Grinspoon.S, and Carr.A. Cardiovascular risk and body-fat abnormalities HIV-Infected adults. N Engl J Med 2005; 352: 48-62.
7. Wanke, Christine A. Epidemiological and clinical aspects of the metabolic complications of HIV infection. The fat redistribution syndrome. AIDS 1999; 13: 1287-1293.
8. Safrin, Sharon, Gurnfeld, Carl. Fat distribution and metabolic changes in patients with HIV infection. AIDS 1999; 13: 2493-2505.
9. Carr, Nadrew. HIV lipodystrophy: risk factors, pathogenesis, diagnosis and management. AIDS 2003; 17: S141-S148.
10. Lichetenstein, Kenneth A et al. Clinical assessment of HIV associated lipodystrophy in an ambulatory population. AIDS 2001; 15:

11. Margaret May, Jonathan A C Sterne, Martin Shipley A coronary heart disease risk model for predicting the effect of potent antiretroviral therapy in HIV-1 infected men89-1398. International Journal of epidemiology 1309- 1318 July 2007
12. D.N. Reeds, B. Mittendorfer, B.W. Patterson, W.G. Powderly, K.E. Yarasheski, and S. Klein Alterations in lipid kinetics in men with HIV dyslipidemia. Am J Physiol Endocrinol Metab, September 1, 2003; 285(3) : E490-497
13. Riddler SA, Smit E, Cole SR, et al. Impact of HIV infection and HAART on serum lipids in men. JAMA 2003; 289: 2978-2982.
14. Grunfeld C, Koler DP et al. Circulating interpheron –alpha levels and hypertrigluceridemia in the acquired immunodeficiency syndrome. J Clin Endocrinol Metab 1992; 74: 1045-1052.
15. .Pang M, Doerrler W, Grunfeld C. Cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Clin Endocrinol Metab 1999; 74: 1045-1052.
16. Mayes P.A., Lipid Transport and Storage. In : Robert KM, Daryl K, Granner, Mayes PA, Rodwell VW, Harper's Biochemistry. 23rd edition. Lange, 1993; 250-265.
17. Genest J, Libby P. Gotto AM Jr. Lipoprotein disorders and Cardiovascular disease In: Zipes, Libby, Bonow, Braunwald. Braunwald's Heart Disease. 7th ed. Elsevier saunders. 2005; 1013-34.
18. Segrest JP. The role of non-LDL : non-HDL particles in atherosclerosis. Curr Diab Rep. 2002 Jun; 2(3) 282-8.
19. J.C. La Rosa; Triglycerides and coronary risk in women and elderly. Arch Intern Med. Vol. 157 No.9, May 12, 1997.

20. Brewer HB Jr, Santamairna-Fojo S. Clinical significance of high-density lipoproteins and the development ofatherosclerosis: focus on the role of the adenosine triphosphate-binding cassette protein A1 transporter.: Am J Cardiol 2003 Aug 21; 92 (4B) : 10K – 16K.
21. Kashyap ML, Tavintharan S, Kamanna VS. Optimal therapy of low levels of high density lipoprotein cholesterol. Am J. Cardiovasc Drugs 2003; 3(1): 53-65.
22. Grunfeld C, Pang M, Doerrler W, Shigenaga JK, Jensen P, Feingold KR. Lipids, lipoproteins, trigluceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Clin Endocrinol Metab 1992; 74: 1045-1052.
23. Hellerstein MK, Grunfeld C, Wu, K et al. Increased de novo hepatic lipogenesis in human immunodeficiency virus infection. J Clin Endocrinol Metab 1993; 76: 559-565.
24. Grunfeld C, Doerrler W, Pang M, Jensen P, Weisgraber KH, Feingold KR. Abnormalities pf apolipoprotein E in the acquired immunodeficiency syndrome. J Clin Endocrinol Metab 1997; 82: 3734-3740.
25. Christeff N, Melchior JC, de Truchis P, Perronne C, Gougeon ML. Increased serum interferon alpha in HIV-1 associated lipodystrophy syndrome. Eur J Clin Invest 2002; 32: 43-50.
26. Lewis GF, Fatty acid regulation of very low density lipoprotein production. Curropin Lipidol 8: 146-156, 1997.
27. Van der Valk M, Reiss P, van Leth FC, Ackermans MT, Endert E, Romijn JA, Heijligenberg R, and Sauerwein J. Highly active antiretroviral therapy-induced lipodystrophy has minor effects on human immunodeficiency virus-induced changes in lipolysis, but

normalizes resting energy expenditure. J Clin Endocrinol Metab 87: 5066-5071, 2002.

28. Renard E, Fabre J, Paris F, Reynes J, and Bringer J, Syndrome of body fat redistribution in HIV-1 infected patients: relationships to cortisol and catecholamines. Clin Endocrinol (Oxf) 51: 223-230, 1999.
29. Kleins S and Wolfe RR. Whole-body lipolysis and triglyceridefatty acid cycling in cachecitc patients with esophageal cancer. J Clin Invest 86: 1403-1408, 1990.
30. Hellerstein MK, Grunfeld C, Wu K, Christiansen M, Kaempfer S, Kletke C, and Shackleton CH. Increased de novo hepatic lipogenesis in human immunodeficiency virus infection. J Clin Endocrinol Metab 76: 559-565, 1993 25.12.1.
31. Baril L, Beucler I, Vlantin MA, Bruckert E, Bonnefont-Rousselot D, Couterllier A, Caumes E, Katlama C, and Bricaire F. Low lipolytic enzyme activity in patients with severe hypertriglyceridemia on higly active antiretroviral therapy. AIDS 15: 415-417, 2001.
32. Sekhar RV, Jahoor F, White AC, Pownall HJ, Visnegarwala F, Rodriguez-Barradas MC, Sharma M, Reeds PJ, and Balasubramanyam A. Metabolic basis of HIV-lipodystrophy syndrome. Am J Physiol Endocrinol Metab 283: E332-E337, 2002.
33. Grunfeld C, Feingold KR. Seminars in medicine of the Beth Israel Hospital, Boston. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. N Engl I Med 1992, 327:329-337.
34. Purnell J, Zambon A, knopp R, et al. Effect of ritonavir on lipids and post-heparin lipase activities in normal subjects. AIDS 2000, 14:51-57.

35. Bastar JP, Caron M, Vidal H, et al. Association between altered expression of adipogenic factor SREBPI in lipoatrophic adipose tissue from HIV-1-infected patients and abnormal adipocyte differentiation and insulin resistance. Lancet 2002; 359: 1026-1031.
36. Caron M, Auclair M, Vigouroux C, Glorian M, Forest C, Capeau J. The HIV protease inhibitor indinavir impairs sterol regulatory element binding protein-1 intranuclear localization, inhibits preadipocyte differentiation, and induces insulin resistance. Diabetes 2001; 50: 1378-1388.
37. Bernasconi E, Boubaker K, Junghans C, et al. Abnormalities of body fat distribution in HIV-infected persons treated with antiretroviral drugs: the Swiss HIV Cohort Study. J Acquir Immune Defic Syndr 2002; 31: 50-55.
38. Miller J,Carr A, Emer S, et al. HIV Lipodystrophy: prevalence, severtity, and correlates of risk n Australia. HIV Med 2003; 4:293-301.
39. Carr A, Samaras K, Thoresdottir A, Kaufmann GR, Chisholm DJ, Cooper DA. Diafnosis, prediction, and natural course of HIV-1 protease-inhibtor-associated lipodystrophy, huperlipidaemia, and diabetes mellitus: a cohort study. Lancet 1999; 352:2093-2009.
40. Gervasion C, Ridolfo Al, Trifiro G, et Redistribution of body fat in HIV- infected women undergoing combined antiretroviral therapy 1999; 13:465-471.
41. Grunfeld C, Basis science and metabolic disturbance. In:program and abstracts of the XIV international AIDS Conference, Barcelona, Spain, July 7-12, 2002: 81 abstract.

42. Carr. A, Emery S, Law M, Puls R, Lundgren JD, Powderly WG. An objective case definition of lipodystrophy in HIV-infecetd adults: a case-control study. Lancet 2003; 361: 726-735.
43. Carr. A, Cooper DA. Lipodystrophy associated with an HIV-protease inhibitor. N Engl J Med 1998; 339: 1296-1296.
44. Mallon PW, Miller J, Cooper DA, Carr, A. Prospective evaluation of the effects of antiretroviral therapy on body composition in HIV –1-infected men starting therapy. AIDS 2003; 17: 971-979.
45. Dube M, Zackin R, Tebas P, et al. Prospective study of regional body composition in antiretroviral –naïve subjects randomized to receive zidovudien + lamivudine or didanosine + stavudine combined with nelfinavir,l efavirenz, or both: A5005s, a study of ACTG 384. Antivir Ther 2002: L18.
46. MArtinex E, Mocroft A, Garcia-Viejo MA, et al. Risk of lipodystriphy in HIV-1-infecetd patients treated with protease inhibitors: a prospective cohort study. Lancet 2001; 357: 592-598.
47. Heath KV, Hogg RS, Singer J, Chan KJ, O'Shaughnessy MV, Montaner JS. Antiretroviral treatment patterns and incident HIV-associated morphologic and lipid abnormalities in a population-based cohort. J Acquir Immune Defic Syndr 2002; 30: 440-447.
48. Caron M, Auclair M, Sterlingot H, Kornprobst M, Capeau J. Some HIV protease inhibitors alter lamin A/c maturation and stability, SREBP-1 nuclear localization and adipocyte differentiation. AIDS 2003; 17: 2437-2444.
49. Reiss P, Casula M, de Ronde A, Weverling G, Goundsmit J, Lange JM. Greater and more rapid depletion of mitochondrial DNA in blood of patients treated with dual (zidovudine + didanosine or zidovudine + zalcitabine) vs. single (zidovudine) nucleoside reverse transcriptase inhibitors. HIV Med 2004; 5: 11-14.

50. Nolan D, Hammond E, Martin A, et al. Mitochondrial DNA depletion and morphologic changes in adipocytes associated with nucleoside reverse transcriptase inhibitor therapy. AIDS 2003; 17: 1329-1338.
51. Pace CS, Martin AM, Hammond EL, Mamotte CD, Nolan DA, Mallal SA. Mitochondiral proliferation, DNA depletion and adipocyte differentiation in subcutaneous adipose tissue of HIV-positive HAART recipients. Antivir Ther 2003; 8: 323-331.
52. Hadigan C, Borgonha S, Rabe J, Yound V, Grinspoon S. Increased rates of lipolysis among human immunodeficiency virus-infected men receiving highly active antiretroviral therapy. Metabolism 2002; 51: 1143-1147.
53. Roche R, Poizot0Martin I, Yazidi CM, et al. Effects of antiretroviral drug combinations on the differentiation of adipocytes. AIDS 2002; 16: 13-20.
54. Galli M, Veglia F, Angarano G, et al. Gender differences in antiretroviral drug-related adipose tissue alterations: women are at higher risk than men and develop particular lipodystrophy patterns. J Acquir Immune Defic Syndr 2003; 34: 58-61.
55. Sutinen J, Hakkinen AM, Westerbacka J, et al. Increased fat accumulation in the liver in HIV-infected patients with antiretroviral therapy associated lipodystrophy. AIDS 2002; 16: 2183-2193.
56. Gan SK, Samaras K, Thompson CH, et al. Altered myocellular and abdominal fat partitioning predict disturbance in insulin action in HIV protease inhibitor related lipodystrophy. Diabetes 2002; 51: 3163-3169.
57. Behrens GM, Boerner AR, Weber K, et al. Impaired glucose phosphorylation and transport in skeletal muscle casue insulin

resistance in HIV-1-infected patients with lipodystrophy. J Clin Invest 2002; 110: 1319-1327.

58. Fauci A S, Lane HC. Human Immunodeficiency Virus Disease: AIDS and related disorders. In : Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL Eds. Harrison's Principles of Internal Medicine. 16th edition, McGraw Hill, NY. 2005; 1120-21.
59. Hadigan C, Meigs JB, Corcoran C, et al. Metabolic abnormalities an cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. Clin Infect Dis 2001; 32: 130-139.
60. Tong Q, Sankale JL, Hadigan CM, et al. Regulation of adiponectin in human immunodeficiency virus-infected patients: relationship to body composition and metabolic indices. J Clin Endocrinol Metab 2003; 88: 1559-1564.
61. Murata H, Hruz PW, Mueckler M. The mechanism of insulin resistance caused by HIV protease inhibitor therapy. J Biol Chem 2000; 275: 20251-20254.
62. Noor MA, Seneviratne T, Aweeka FT, et al. Indinavir acutely inhibits insulin-stimulated glucose disposal in humans; a randomized, placebo-controlled study. AIDS 2002; 16: F1-F8.
63. Lee GA, Seneviratne T, Noor MA, et al. The metabolic effects of lopinavir/ ritonavir in HIV-negative men. AIDS 2004; 18: 641-649.
64. Woerle HJ, Mariuz PR, Meyer C, et al. Mechanisms for the deterioration in glucose tolerance associated with HIV protease inhibitor regimens. Diabetes 2003; 52: 918-925.
65. Klein D, Hurley LB, Quesnberry CP Jr, Sidney S. Do protease inhibitors increae the risk for coronary heart disease in patients

with HIV-1- Infection? J Acquir Immune Defic Syndr 2002; 30: 471-477.

66. The Data Collection on Adverse Events of Anti-HIC Drugs (DAD) Study Group. Combination antiretroviral therapy and the risk of myocardial infarction. N Engl J Med 2003; 349: 1993-2003.
67. Feingold KR, Krauss RM, Pang M, Doerrler W, Jensen P, Grunfeld C. The hypertrigluceridemia of acquired immunodeficiency syndrome is associated with an increased prevalence of low density lipoprotein subclass pattern B. J Clin Endocrinol Metab 1993; 76: 1423-1427.
68. Hause PY, Lo JC, Franklin A, et al. Progression of atherosclerosis as assessed by carotid intimamedia thickness in patients with HIV infection. Circulation 2004; 109: 1603-1608.
69. Stein JH, Klein MA, Bellehumeur JL, et al. Use of human immunodeficiency virus-1 protease inhibitors is associated with atherogenic lipoprotein changes and endothelial dysfunction. Circulation 2001; 104: 257-262.
70. Friis-Moller N, Weber R, Reiss P, et al. Cardiovascular disease risk factors in HIV patients association with antiretroviral therapy; results from the DAD study. AIDS 2003; 17: 1179-1193.
71. Dressman J, Kincer J, Matveev SV, et al. HIV protease inhibitors promote atherosclerotic lesion formation independent of dyslipidemia by increasing CD36-dependent cholesteryl ester accumulation in macrophages. J Clin Invest 2003; 111: 389-397.
72. Perry RC, Cushing HE, Deeg MA, Prince MJ. Ritonavir, triglycerides and pancreatitis. Clin Infect Dis 1999, 28: 161-162.
73. Stricker RB, Man KM, Bouvier DB, Goldber DA, Mendiola AE. Pancreatorenal syndrome associated with combination

antiretroviral therapy in HIV infection. Lancet 1997, 349: 1745-1746.

74. Miller J, Brown D, Amin J, et al. A randomized, double-blind study of gemfibrozil for the treatment of protease inhibitor associated hypertrigluceridaemia. AIDS 2002; 16: 2195-2200.
75. Moyle GJ, Lloyed M, Reynolds B, Baldwin C, Mandalia S, Gazzard BG. Dietary advice with or without pravastatin for the management of hypercholesterolaemia associated with protease inhibitor therapy. AIDS 2001; 15: 1503-1508.
76. Calza L, Manfredi R, Chiodo F. Statins and fibrates for the treatment of hyperlipidaemia in HIV infected patients receiving HAART. AIDS 2003; 17: 851-859.
77. Fichtenbaum CJ, Gerber JG, Rosenkranz SL, et al. Pharmacokinetic interactions between protease inhibitors and statins in HIV seronegative volunteers: ACTG Study A5047. AIDS 2002; 15: 569-577.
78. Hadigan C, Meigs JB, Rabe J, et al. Increased PAI-1 and tPA antigen levels are reduced with metformin therapy in HIV-infected patients with fat redistribution and insulin resistance. J CLin Endocrinol Metab 2001; 86: 939-943.
79. Hadigan C, Corcoran C, Basgoz N, Davis B, Sax P, Grinspoon S. Metformin in the treatment of HIV lipodystrophy syndrome: a randomized controlled trial. JAMA 2000; 284: 472-477.
80. Arioglu E, Duncan-Morin J, Sbring N, et al. Efficacy and safety of troglitazone in the treatment of lipodystrophy syndromes. Ann Intern Med 2000; 133: 263-274.
81. Sutinen J, Hakkinen AM, Westerbacka J, et al. Rosiglitazone in the treatment of HAART associated lipodystrophy – a randomized

double blind placebo controlled study. Antivir Ther 2003; 8: 199-207.

82. Hadigan C, Yawetz S, Thomas A, Havers F, Sax PE, Grinspoon S. Metabolic effects of rosiglitazone in HIV lipodystrophy: a randomized, controlled trial. Ann Intern Med. 2004; 140: 786-794.
83. Carr A, Workman C, Carey D, et al. No effect of rosiglitazone for treatment of HIV-1 lipoatrophy: randomized, double-blind, placebo-controlled trial. Lancet 2004; 363: 429-438.
84. Calmay A, Hirschel B, Hans D, Karsegard VL, Meier CA. Glitazones in lipodystrophy syndrome induced by highly active antiretroviral therapy. AIDS 2003; 17: 770-772.
85. Gelato MC, Mynarcik DC, Quick JL, et al Improved insulin sensitivity and body fat distribution in HIV-infected patients treated with rosiglitazone: a pilot study. J Acquir Immune Defic Syndr 2002; 31: 163-170.
86. Engelson ES, Glesby MJ, Mendez D, et al. Effect of recombinant human growth hormone in the treatment of visceral fat accumulation in HIV infection. J Acquir Immune Defic Syndr 2002; 30: 379-391.
87. Koteler DP, MuurahainenN, Grunfeld C, et al. Effects of growth hormone on abnormal visceral adipose tissue accumulation and dyslipidemia in HIV infected patients. J Acquir Immune Defic Syndr 2004; 35: 239-252.
88. Koutkia P, Canavan B, Breu J, Torriani M, Kissko J, Grinspoon S. Growth hormone-releasing hormone in HIV-infected men with lipodystrophy: a randomized, controlled trial. JAMA 2004; 292: 210-218

89. Moyle GJ, Lysakova L, Brown S, et al. A randomized open label study of immediate versus delayed polyactic acid injections for the cosmetic management of facial lipoatrophy in persons with HIV infection. HIV Med 2004; 5: 82-87.
90. Martinez E, Arniaz JA, Podzamczer D, et al. Substitution of nevirapine, efavirenz, or abacavir for protease inhibitors in patients with human immunodeficiency virus infection. N Engl J Med 2003; 349: 1036-1046.
91. Martinez E, COnget I, Lozano L, Casamitjana R, Gatell JM. Reversion of metabolic abnormalities after switching from HIV-1 protease inhibitors to nevirapine. AIDS 1999; 13: 805-810.
92. Moyle GJ, Baldwin C, Langroudi B, Mandalia S, Gazzard BG. A 48-week, randomized, open-label comparison of three abacavir-based substitution approaches in the management of dyslipidemia and peripheral lipoatrophy. J Acquir Immune Defic Syndr 2003; 33: 22-2.
93. Negredo E, Ribalta J, Paredes R, et al. Reversal of atherogenic lipoprotein profile in HIV-1 infected patients with lipodystrophy after replacing protease inhibitors by nevirapine. AIDS 2002; 16: 1383-1389.
94. Caan B, Armstrong MA, Selby JV, et al. Changes in measurements of body fat distribution accompanying weight change. Int. J Obes Relat Metab Disord 1994, 18: 397-404.
95. API ART Guidelines 2007 JAPI 2007
96. Leonardo Calza; Roberto Manfredi; Vincenzo Colangeli Substitution of Nevirapine or Efavirenz for Protease Inhibitor Versus Lipid-Lowering Therapy for the Management of Dyslipidemia AIDS Journal 2003 vol 17

97. DAD Study group Nina Friis Moller, Jens Lundgren and et al N Engl J Med 2007; 356:1723-1735, Apr 26, 2007.
98. Sharon A. Riddler, Ellen Smit; Impact of HIV Infection and HAART on Serum Lipids in Men ,JAMA. 2003; 289(22):2978-2982
99. Joel E. Gallant; Schlomo Staszewski; Anton L. Pozniak; et al. JAMA. 2004;292(2):191-201Efficacy and Safety of Tenofovir DF vs Stavudine inCombination Therapy in Antiretroviral-Naive Patients: A 3-Year Randomized Trial
100. Prevalence of Metabolic Syndrome in HIV Infected Patients Receiving Highly Active Antiretroviral Therapy Using International Diabetes Foundation and Adult Treatment Panel III Criteria Katherine Samaras, Handan Wand et al Diabetes Care 30: 113- 119
101. G Baril, P Junod, R LeBlanc, et al. HIV-associated lipodystrophy: A review of clinical aspects. Can J Infect Dis Med Microbiol 2005;16(4):233-243

GLOSSARY

1. HIV – Human Immuno deficiency Virus
2. AIDS- Acquired Immuno deficency Syndrome
3. HAART- Highly Active Anti Retroviral Therapy
4. ART- Anti Retroviral Therapy
5. NRTI- Nucleoside Reverse transcriptase inhibitor
6. NNRTI-Non Nucleoside Reverse transcriptase inhibitor
7. PI-Protease Inhibitor
8. PLHA-People Living with HIV and AIDS
9. NACO- National AIDS Control Organisation
10. D4T- Stavudine
11. 3TC- Lamuvidine
12. CAD – Coronary Artery Disease
13. INF- α- Interferon Alpha
14. TNF α- Tumor Necrosis Factor Alpha
15. SREBPI- Sterol Regulatory Enhancer-Binding Protein-1(SREBPI)
16. PLAH – People Living with HIV and AIDS
17. PPARγ- Peroxisome Proliferatory Receptor Gamma.
18. STD -Sexually Transmitted Diseases

PROFORMA

Dyslipidemia in HIV patients on HAART and Treatment naïve

HIV patients

Name Age Sex

IP No: Occupation

Marital status WHO stage

Educational status

Clinical status

H/o IHD

Diabeties

CVA

Hypertension

POVD

Personal History

Smoking ; Y/N Duration Packs/Day

Alcohol :Y/N Duration

Diet : Veg / Non veg

Family History

Diabeties : Y/N

IHD : Y/N

Examination

Height Weight BMI

WC HC WC/HC

Pulse Rate BP Respiratory rate

Systems

Cardiovascular

Respiratory

Nuerological status

GIT

Treatment Groups

1. Lamuvidine/Staudine/Nevirapine
2. Lamuvidine/Stuvidine / Efavirenz
3. Lamuvidine/ Zidovudine/ Nevirapine
4. Lamivudine/Zidovudine/Efavirenz
5. HAART naïve patients

Investigations

1 Urine Albumin 2 Spot PCR

Sugar

Deposits

3 Fasting blood sugar 4 2hr Postprandial

5 Blood Urea Serum Creatinine

6 Lipid Profile

Total Cholesterol

Triglycerides

HDL

VLDL

LDL

7 LFT

8 CD 4 Count

9. ECG

MASTER CHART

SL.NO	SEX	GROUP	AGE	BMI	W/C	HTN	TC	TGL	LDL	HDL	VLDL	IFG/IGT	SMOKING	IHD	ALCOHOLISM	CD4
1	F	5	35	18	0.9	2	148	210	71	32	44	3	0	2	0	230
2	F	5	33	17.5	0.85	2	169	125	100	42	25	3	0	2	0	212
3	F	5	29	19	0.83	2	172	139	104	40	28	3	0	2	0	450
4	F	5	42	24	0.8	2	168	270	77	41	54	3	0	2	0	85
5	M	5	35	18.5	0.78	2	186	235	106	21	47	3	1	2	0	175
6	F	5	35	19	0.81	2	154	185	78	35	37	3	0	2	0	294
7	M	5	28	19	0.93	2	166	143	96	41	29	3	2	2	1	330
8	M	5	39	22	0.94	1	160	219	80	36	44	3	2	2	0	38
9	F	5	25	20	0.88	2	165	142	100	32	28	3	0	2	0	402
10	M	5	42	18	0.87	2	193	285	105	31	57	1	1	1	1	232
11	M	5	33	19	0.86	2	177	173	99	41	35	3	1	2	1	256
12	M	5	37	22	0.98	2	181	142	118	30	28	3	2	2	0	330
13	M	5	25	21	0.91	2	156	138	72	42	28	3	2	2	0	177
14	F	5	29	19	0.93	2	152	163	78	43	33	3	0	2	0	156
15	F	5	44	20	0.91	2	189	148	109	41	30	3	0	2	0	267
16	M	5	26	23	0.94	1	225	331	127	32	65	3	0	2	1	21
17	F	5	28	21	0.81	2	171	139	99	42	28	3	2	2	0	332
18	F	5	29	19	0.82	2	146	187	69	40	36	3	0	2	0	238
19	F	5	31	22	0.78	2	138	147	68	41	30	3	0	2	0	145
20	M	5	37	20	0.92	2	200	278	110	30	56	3	0	2	0	247
21	M	5	44	17	0.97	2	165	302	67	34	60	3	2	2	1	209
22	M	5	33	19	0.87	2	169	119	103	41	24	3	2	2	1	265
23	M	5	39	16	0.82	2	129	86	72	40	17	3	1	2	1	198
24	M	5	28	17	0.86	2	152	113	88	41	22	3	1	2	0	245
25	F	5	36	21	0.91	2	153	230	73	34	46	3	0	2	0	268
26	F	5	25	20	0.93	2	152	108	88	42	22	3	0	2	0	275
27	F	5	29	18	0.81	2	159	132	95	35	26	3	0	2	0	91
28	M	5	27	18	0.91	2	149	109	87	40	21	3	1	2	1	241

29	F	5	39	19.5	0.84	2	160	186	85	32	35	3	0	2	0	245
30	M	5	42	21	0.9	1	242	385	133	32	77	1	2	2	1	40
31	M	5	40	16	0.88	2	231	275	141	30	55	3	2	2	1	256
32	F	5	41	18	0.79	2	176	149	106	40	30	3	0	2	0	132
33	M	5	45	20	0.99	2	173	188	101	31	38	3	1	2	0	85
34	F	5	39	21	0.86	2	149	126	78	42	25	3	1	2	0	288
35	F	5	40	18	0.85	1	167	317	70	34	63	3	1	2	0	298
36	M	5	36	19	0.86	2	160	138	93	39	28	3	1	2	1	47
37	M	5	28	19	0.76	2	177	98	110	47	20	3	2	2	1	188
38	M	5	29	18	0.97	2	134	129	70	38	26	3	1	2	1	311
39	F	5	28	17	0.84	2	169	193	95	35	39	3	0	2	0	404
40	F	5	24	19	0.81	2	109	122	44	41	24	3	0	2	0	120
41	F	5	38	21	0.91	1	246	200	171	35	40	2	0	2	0	221
42	F	5	25	21	0.8	2	116	121	50	41	24	3	0	2	0	293
43	M	5	26	21	0.85	2	155	141	87	40	28	3	2	2	1	357
44	F	5	27	23	0.9	2	114	172	42	38	34	3	2	2	0	217
45	F	5	32	22	0.91	2	208	175	139	34	35	3	0	2	0	125
46	M	5	41	19	0.85	1	253	229	172	35	46	3	1	2	1	285
47	M	5	43	18	0.96	2	170	245	81	40	49	3	1	1	1	165
48	F	5	35	19	0.88	2	159	128	88	46	26	3	0	2	0	35
49	F	5	36	21	0.83	2	123	85	66	38	17	3	0	2	0	244
50	F	5	37	20	0.79	2	168	96	108	40	19	3	0	2	0	234
51	M	5	38	20	0.89	2	177	189	104	35	38	3	0	2	1	355
52	M	5	32	19	0.89	2	190	210	109	39	42	3	1	2	1	123
53	F	5	25	21	1.01	2	160	138	95	37	28	3	0	2	0	267
54	F	4	3O	18	0.89	2	240	185	165	38	37	3	0	2	0	302
55	F	1	43	19	0.99	2	223	236	142	34	47	3	0	2	0	227
56	M	2	44	17	1.04	1	270	247	189	32	49	3	2	1	0	367
57	M	3	28	21	0.9	2	175	139	106	41	28	3	1	2	0	225
58	M	3	37	20	1.1	2	186	167	112	41	33	2	0	2	0	210
59	M	1	35	17	0.96	2	176	199	104	32	40	3	2	2	0	145
60	F	4	38	15	0.96	2	289	255	199	39	51	3	0	2	0	97
61	M	2	42	18	0.96	2	256	200	179	37	40	3	2	1	0	108

62	F	3	41	19	0.95	2	192	317	95	34	63	1	0	2	0	105
63	F	2	39	17	0.96	2	231	178	183	33	26	3	0	2	0	54
64	M	3	33	20	0.88	2	185	147	101	37	29	3	1	2	0	43
65	F	3	30	21	0.92	2	183	127	111	39	25	3	1	2	0	165
66	M	2	28	26	0.88	2	276	321	176	36	64	3	2	2	1	383
67	M	4	32	20	0.89	2	198	143	131	38	28	3	2	2	1	165
68	F	3	39	18	0.93	2	154	184	79	38	37	3	0	2	0	208
69	F	1	39	19	1.03	2	209	147	139	41	30	3	0	1	0	245
70	M	3	40	18	0.98	2	217	277	127	35	56	3	2	2	1	166
71	M	2	42	22	1.04	1	239	178	170	35	35	3	2	2	0	208
72	M	2	29	19	0.96	2	270	365	165	32	73	3	2	2	0	76
73	M	4	33	18	0.94	2	206	237	126	33	47	3	1	2	1	103
74	F	2	41	19	0.89	2	277	409	162	33	82	3	0	2	0	65
75	F	3	32	18	0.93	2	174	127	101	48	25	3	0	2	0	111
76	M	2	36	19	0.94	2	276	142	214	33	28	2	0	2	0	208
77	F	4	39	20	1.1	1	227	291	129	33	58	3	0	1	1	221
78	M	3	29	17	0.88	2	179	147	103	47	29	3	1	2	0	109
79	M	2	22	18	1.06	2	287	307	190	35	62	3	1	2	0	105
80	F	1	37	20	0.98	2	238	146	168	41	29	3	0	2	0	49
81	F	4	36	18	1.01	1	215	285	134	39	57	3	0	2	0	77
82	M	1	28	18	0.99	2	204	257	116	36	52	3	2	2	0	83
83	M	4	44	19	0.9	2	230	233	150	34	47	3	2	2	0	45
84	F	4	44	18	0.89	1	222	285	132	33	57	3	0	1	0	39
85	F	3	39	20	0.86	2	169	139	99	42	28	3	0	2	0	152
86	M	3	42	21	0.95	2	195	241	112	35	48	3	1	2	0	109
87	M	1	26	22	1.06	2	166	179	91	39	36	3	1	2	0	217
88	M	2	38	21	0.92	2	154	187	141	48	25	3	0	2	0	235
89	F	3	36	17	0.94	2	189	239	110	32	48	3	0	2	0	208
90	F	1	30	19	0.88	2	195	176	124	35	35	3	0	2	0	214
91	M	4	29	20	0.93	2	217	129	150	42	26	3	2	2	0	231
92	M	2	32	23	0.96	2	295	176	225	35	35	2	2	2	0	188
93	F	2	32	21	0.95	2	262	288	171	33	58	3	0	2	0	197

94	M	3	24	21	0.96	2	186	247	94	34	49	1	2	1	0	201
95	M	2	43	20	0.95	2	228	157	152	45	32	3	2	2	0	223
96	M	4	36	18	0.98	2	218	211	138	37	42	3	2	2	1	95
97	F	4	29	19	0.97	2	200	239	119	33	48	3	0	2	0	46
98	M	3	33	18	0.88	1	172	119	106	42	24	3	2	2	0	104
99	M	4	41	21	1.09	2	214	267	126	34	53	3	2	2	0	138
100	M	2	37	24	0.89	2	245	365	131	31	73	2	2	1	0	179
101	M	1	31	18	0.89	2	178	147	106	42	28	3	1	2	0	188
102	M	2	22	21	1.07	2	265	189	190	37	38	2	1	1	1	195
103	M	1	42	21	1.03	1	177	169	107	36	34	3	1	2	0	266
104	M	2	38	18	0.91	2	198	241	167	34	48	3	2	2	0	200
105	F	4	36	17	0.8	2	178	163	105	40	33	3	0	1	0	179
106	F	2	40	20	0.91	2	199	124	129	45	25	3	0	2	0	175
107	M	2	31	20	0.96	2	238	222	156	38	44	3	2	2	0	44
108	M	1	35	21	0.94	2	205	169	136	33	34	3	2	2	1	65
109	F	1	31	26	0.89	1	241	313	144	34	63	2	0	2	0	117
110	M	2	37	20	1.06	2	254	266	166	35	53	3	1	2	0	368
111	F	3	25	19	0.96	2	169	98	106	43	20	3	0	1	0	135
112	F	4	38	19	1.01	2	206	183	134	36	35	3	0	2	0	199
113	M	2	36	18	1.05	2	257	276	168	34	55	3	2	2	1	265
114	M	4	44	21	0.96	2	239	298	144	35	59	3	2	2	0	177
115	M	4	42	21	0.99	2	229	368	123	33	74	3	2	2	0	109
116	F	2	39	18	0.86	2	241	206	171	39	41	3	0	2	0	169
117	M	2	43	17	0.84	2	205	122	146	45	24	3	0	2	0	188
118	F	3	33	19	0.88	2	170	196	96	35	39	3	0	2	0	178
119	F	3	27	18	0.92	2	160	138	94	37	28	2	0	2	0	249
120	M	1	36	18	0.94	2	163	187	90	37	37	3	2	2	0	199
121	M	2	36	19	1.07	2	254	317	159	32	64	3	2	2	0	167
122	M	3	40	21	0.96	2	152	114	84	41	23	3	2	1	0	77
123	M	2	42	21	0.96	2	227	139	160	39	28	3	2	1	0	139
124	M	2	37	18	1.04	1	208	175	139	34	35	3	1	2	0	266
125	M	1	29	21	0.9	2	177	112	114	41	22	3	1	2	0	145
126	F	4	30	20	0.81	2	216	145	148	39	29	3	0	2	0	97

KEYS TO MASTER CHART

Variables

SEX

M- Male

F – Female

S- Smoking

0-non smoker

1-smoker

2-quit smoking

BMI- Body mass index

W/H – Waist Hip ratio

HTN-

1- Hypertensive

2- Normotensive

IFG/IGT – Impaired Fasting Glucose / Impaired Glucose Tolerance

1- IFG Detected

2- IGT Detected

3 - No IFG and IGT

G-Group

1 -D4T+3TC+NVP

2 -D4T+3TC+EVF

3 -ZVD+3TC+NVP

4 -ZVD+3TC+ EVF

5 -HIV not on ART

A- ALOCHOLIC

0- NON ALCOHOLIC

1-ALOCHOLIC

IHD-Ischemic heart disease.

1- no heart disease

2- present

TC.-Total cholesterol

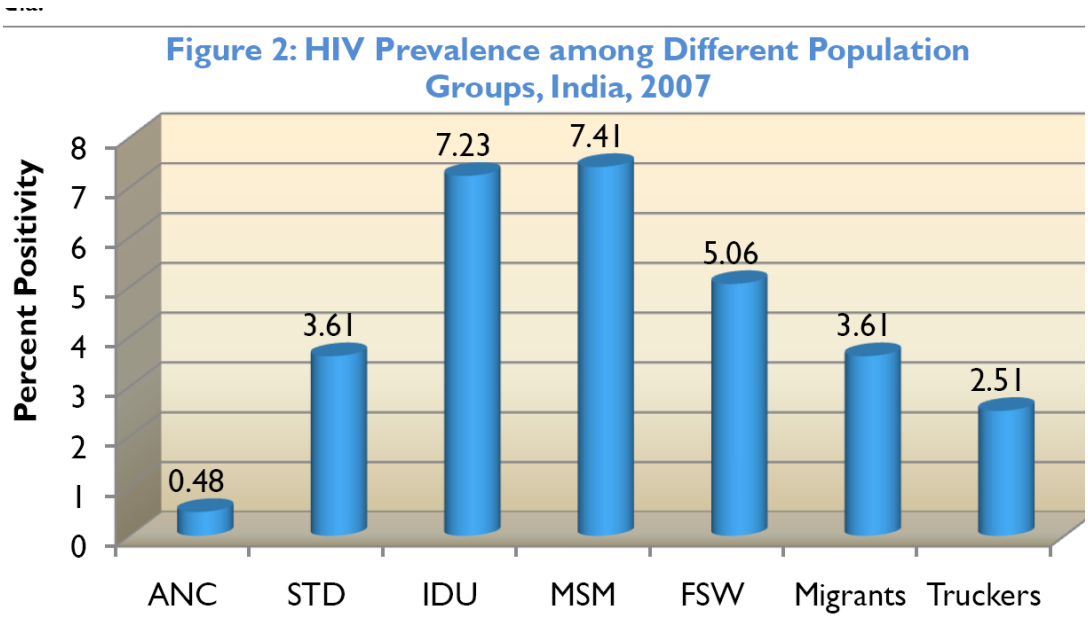
TGL- Triglycerides

LDL-Low density lipoprotein

VLDL-very low density lipoprotein

PREVALENCE OF HIV IN DIFFERENT GROUPS IN INDIA

Fig 2



ANC- Antenatal Clinics STD – Sexually Transmitted Disease Clinics

IDU – Injectable Drug Abusers .MSM- Male Sex with Male

FSW- Female Sex Workers. Prevalence in percentage.

MECHANISM OF DYLIPDIEMIA IN HIV PATIENTS AND HAART

Fig 3

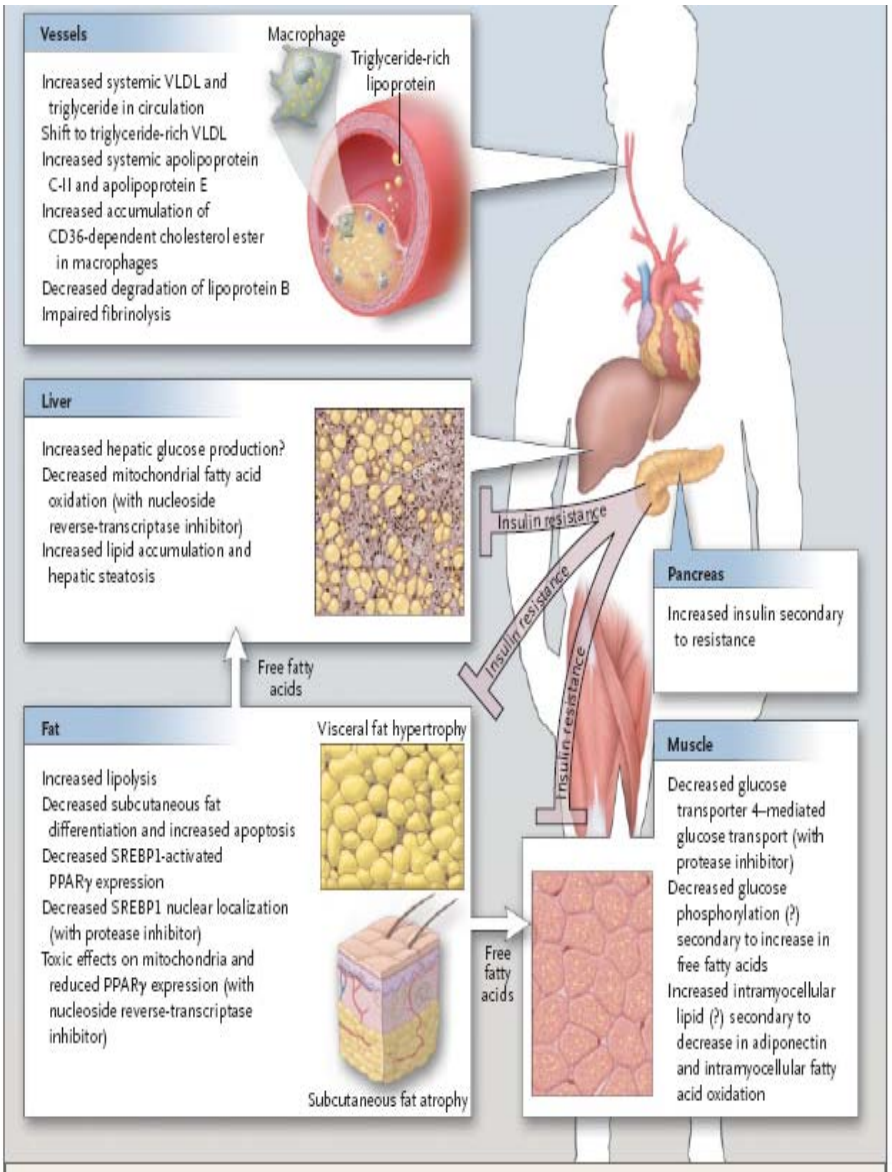
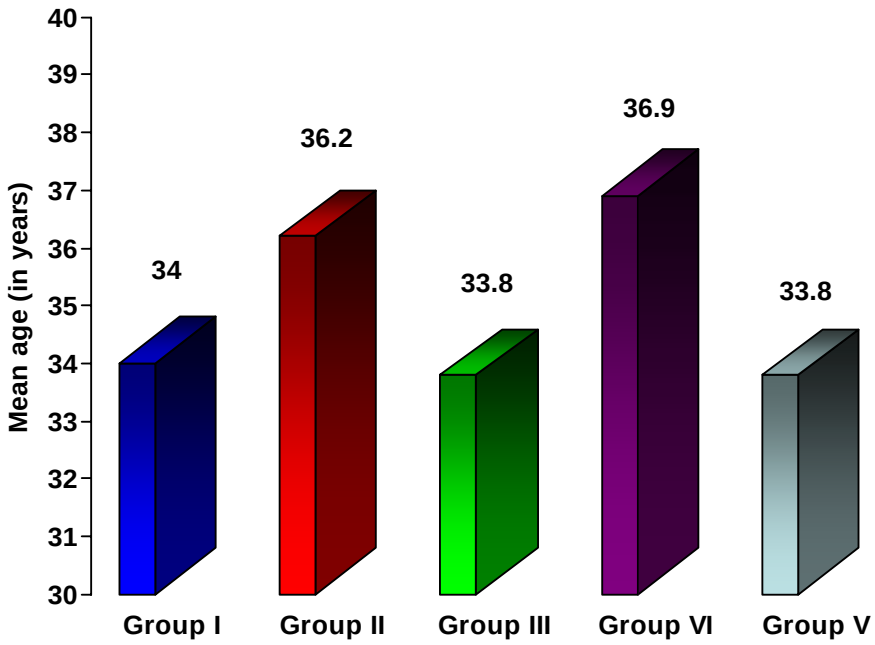


Figure 2. Potential Mechanisms for Metabolic Abnormalities in HIV-Infected Patients Receiving Highly Active Antiretroviral Therapy.

Individual drugs within each class may have various effects. Drugs may differentially affect fat depots, with protease inhibitors and nucleoside reverse-transcriptase inhibitors decreasing differentiation and adipogenesis in subcutaneous fat. Relative or absolute increases may occur in visceral fat independently of changes in subcutaneous fat. The specific causes of visceral-fat hypertrophy are not yet known. The development of metabolic abnormalities may be affected by genetic background as well as age, environmental factors, and other medications used. VLDL denotes very-low-density lipoprotein, SREBP1 sterol regulatory enhancer–binding protein 1, and PPARγ peroxisome proliferator–activated receptor γ.

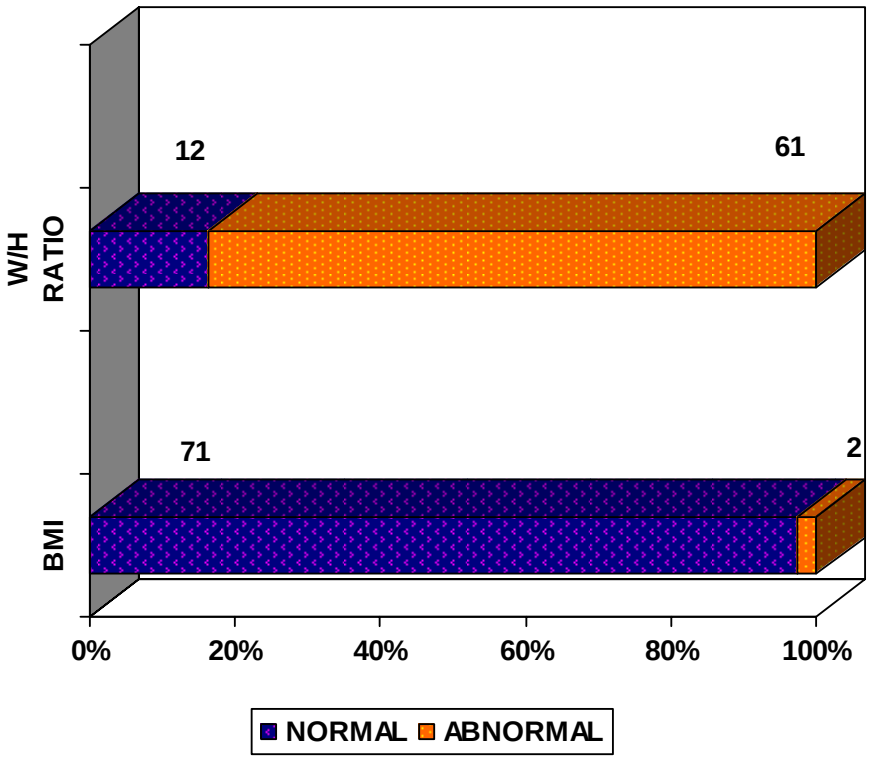
DISTRIBUTION OF MEAN AGE AMONG STUDY GROUPS I-IV

Fig-4



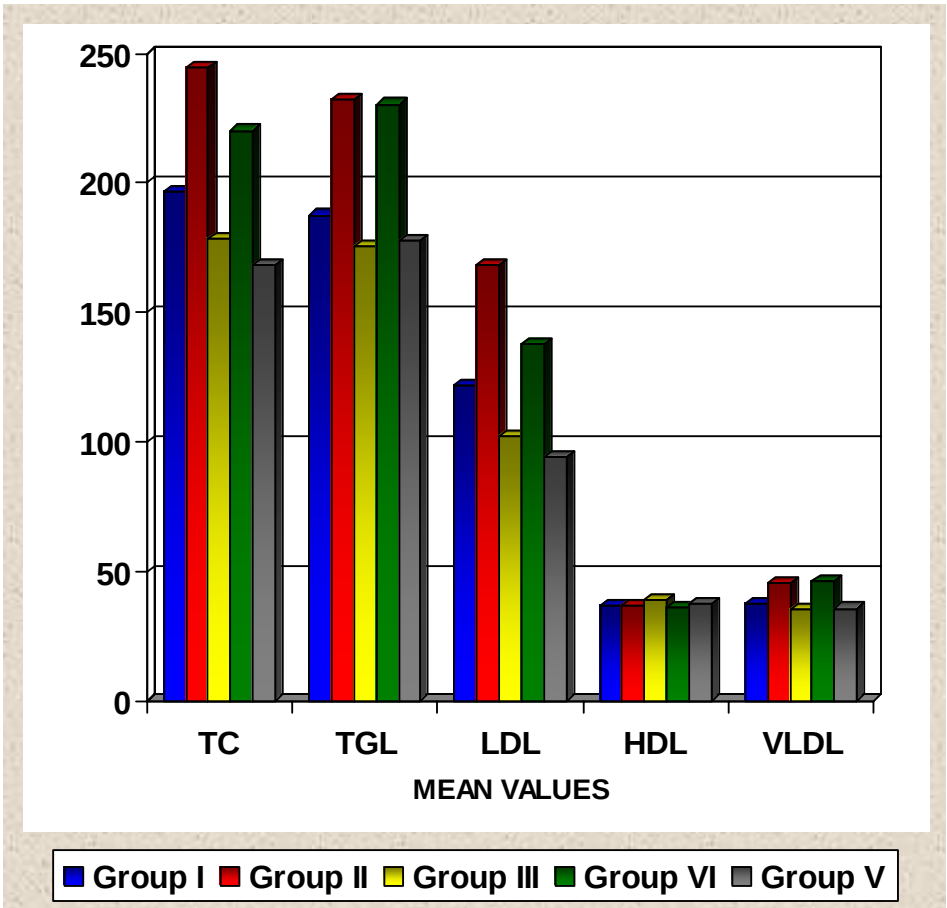
WAIST/ HIP RATIO AND BMI

Fig -6



MEAN LIPID VALUES OF THE STUDY GROUPS. I-V

Fig- 7



CARDIOVASCULAR RISK IN HIV PATIENTS ON HAART DAD STUDY GROUP

Fig -9

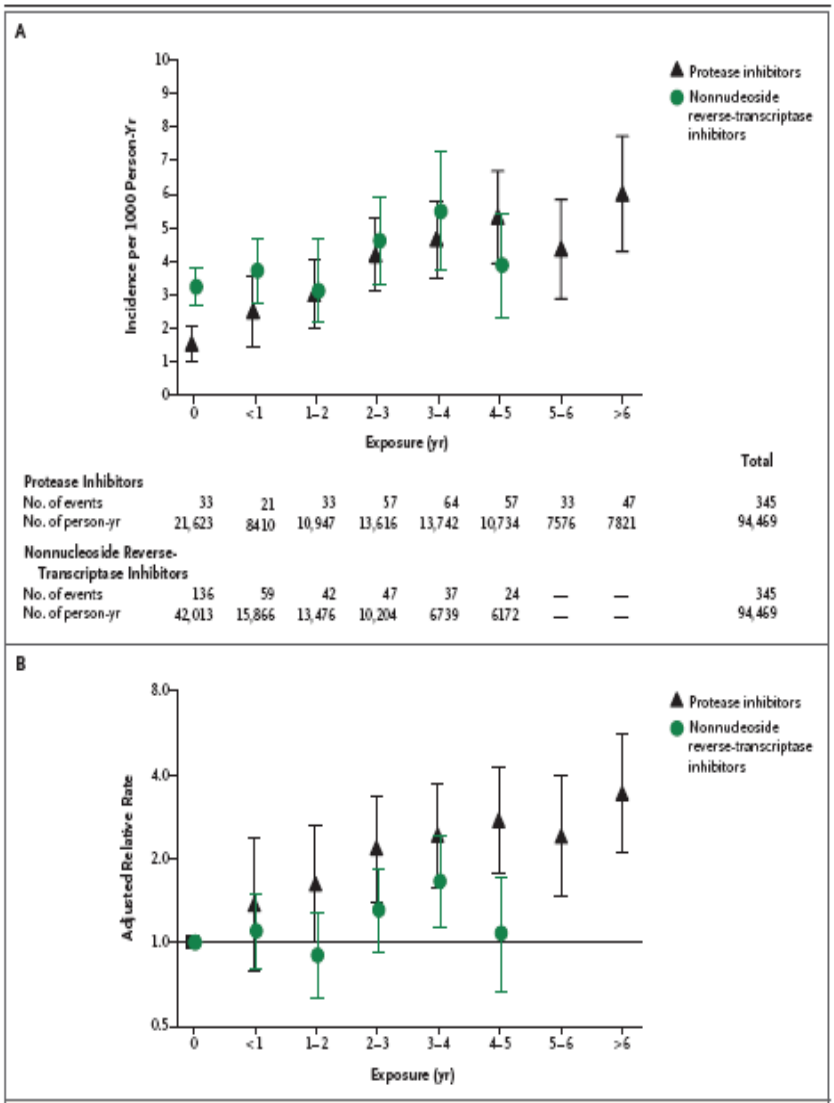
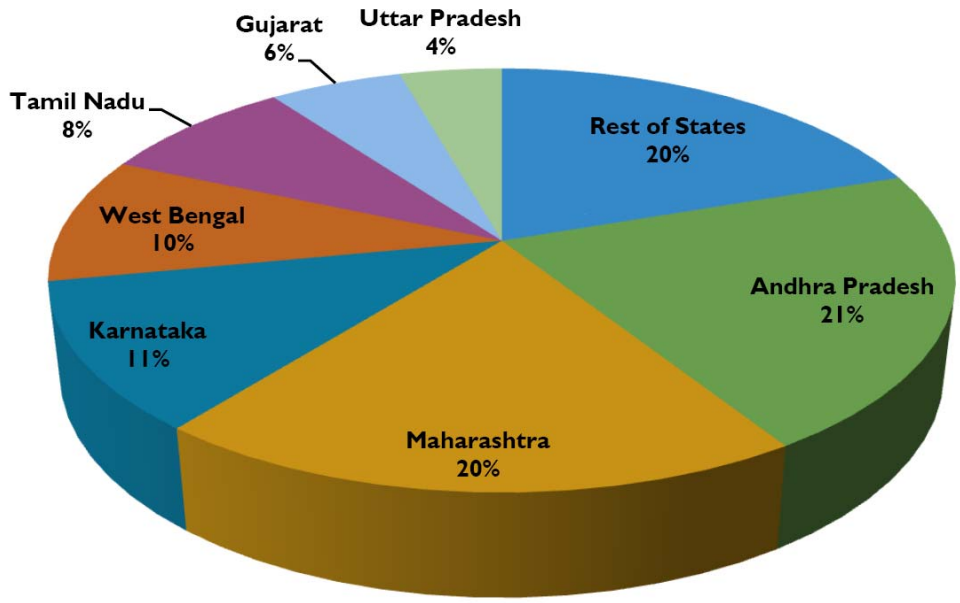


Figure 2. Risk of Myocardial Infarction According to Exposure to Protease Inhibitors and Nonnucleoside Reverse-Transcriptase Inhibitors.

Cumulative exposure was categorized as no exposure, less than 1 year, 1 to 2 years, 2 to 3 years, 3 to 4 years, 4 to 5 years, 5 to 6 years, and more than 6 years for protease inhibitors and as no exposure, less than 1 year, 1 to 2 years, 2 to 3 years, 3 to 4 years, and more than 4 years for nonnucleoside reverse-transcriptase inhibitors. Panel A shows the incidence of primary events according to the cumulative exposure to protease inhibitors and nonnucleoside reverse-transcriptase inhibitors. Panel B shows the adjusted relative rates of myocardial infarction according to the cumulative exposure to protease inhibitors and nonnucleoside reverse-transcriptase inhibitors. The estimates were based on Poisson regression models. The multivariable model was adjusted for sex, cohort, HIV transmission group, race or ethnic group, age, body-mass index, family history of cardiovascular disease, smoking status, previous cardiovascular event, and calendar year. The sum of the person-years may not total 94,469 because of rounding. The I bars denote the 95% CIs.

PREVALENCE OF HIV IN DIFFERENT STATES IN INDIA -2007

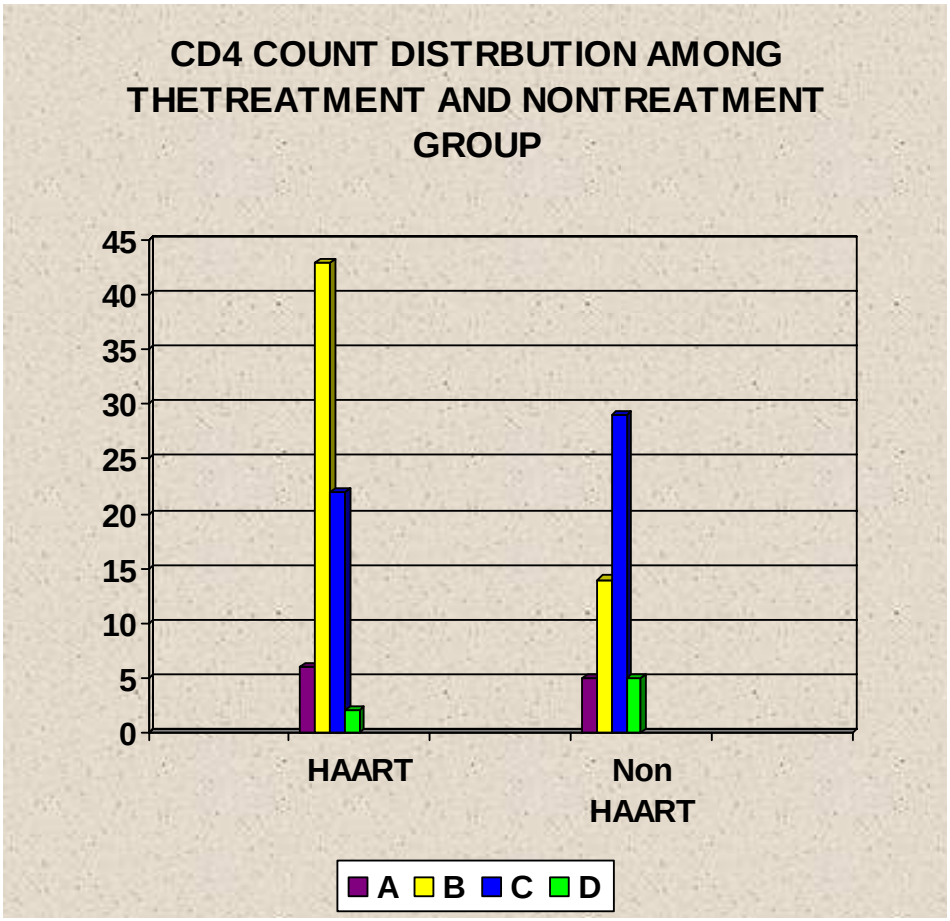
Fig-1



South Indian States of Karnataka, Tamil Nadu ,Andhra Pradesh & Maharashtra constitutes 60% of the total cases . Manipur and Nagaland accounts for the maximum prevalence of HIV infection in India[2].

CD-4 CELL COUNT AMONG HAART AND NON HAART GROUPS

Fig -5



SEVERE LIPOATROPHY OF FACE IN A PATIENT WITH AIDS

Fig-8